201-16251

May 4th, 2006

Attn: Chemical Right-to-Know Program
Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
(email: oppt.ncic@epa.gov, chem.rtk@epa.gov)

RE: Submission for HPV Challenge Program -- DEA

Dear Sir or Madam:

Albemarle Corporation (sponsor registration) is pleased to submit the attached Category Justification, Robust Summary, and Test Plan documents (in Word ".doc" format) for the "Ring Substituted Anilines Category" category of compounds (covered by the HPV chemical "2,6-Diethylaniline" with CAS# 579-66-8, and EHPV chemical "Ortho-Ethylaniline" with CAS# 578-54-1), as a voluntary participant in the HPV Challenge Program and as part of our ongoing commitment to product stewardship. Supporting documentation (in Word ".doc" and ".pdf" formats) on related anilines; "Aniline" and "2,6-Methyl Ethyl Aniline"; is also included in order to provide a more complete understanding of this category.

As referenced in our December 28, 2005 commitment letter and March 31, 2006 communication update to the HPV Challenge program, we understand that EPA will continue to recognize these as viable commitments, and that if necessary, additional testing will be conducted in the time frame established by the US EPA HPV Challenge Program. We also understand that the information and data we provide under the HPV Challenge Program will be reviewed and made publicly available.

The technical contact for this submission to the U.S. EPA HPV program is:

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Sincerely,

Len Sweet, PhD, MPH
Global Product Stewardship Director


Aniline categoryHPV.doc
anilinedataset_hpv.doc
DEAluclidHPV.doc
OEAluclidHPV.doc
MEAluclidsuppHPV.doc
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2,6 Diethyl Aniline and Ortho ethyl aniline: Ring-substituted Monocyclic Aromatic Amines Category Justification and Testing Rationale

CAS 57466-8 and 578-54-l
(Plus SIDS/ICCA Chemicals 62-53-3 and 2454906-2 for reference)

I. INTRODUCTION

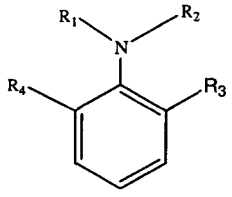
Albemarle Corporation (Albemarle) would like to submit a test plan for 2,6 diethyl aniline (2,6 DEA) in the Environmental Protection Agency's High Production Volume (HPV) Challenge Program and for ortho ethyl aniline, listed as an Extended High Production Volume chemical.

Albemarle is committed to making existing test data publicly available for these chemicals and to develop any additional screening level data needed on health and environmental effects, fate, and physiochemical properties. In order to minimize the use of animals in the testing of chemicals, Albemarle has conducted a thorough literature search for all available data, published and unpublished for 2,6 DEA and related alkyl substituted aromatic amines. It also has performed an analysis of the adequacy of the existing data. Further, it developed a scientifically supportable category of related chemicals and used structure-activity relationship information as appropriate. No testing of whole animals is proposed. This document describes the alkyl substituted aniline 2,6 DEA, included in the HPV program, ortho ethyl aniline (OEA), included as an "Extended HPV" chemical and notes the related chemicals that are being sponsored through the OECD SIDS program (aniline, 2,6 MEA). This is similar to the approach used by the Monocyclic Aromatic Amines and Nitroaromatics (MAANA) Panel and its member companies for monocyclic aromatic amines with nitrogen substituents previously. Data on all these chemicals are included to provide justification for the proposed category. Robust summary documents have been prepared and are included for each of these chemicals (aniline document from the MAANA panel, 2,6 methyl ethyl aniline IUCLID from the European Chemical Bureau files). Finally, the rationale for proposed testing is described.

II. DEVELOPMENT OF THE Ring-substituted Anilines CATEGORY

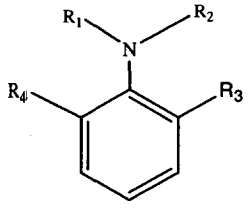
All chemicals included in this plan are monocyclic aromatic amine compounds, with aniline as the parent chemical. These substituted anilines all have a single amino group and also have one or more methyl or ethyl substituents on the aromatic ring. Figure 1 gives the names, CAS numbers, and structures of the compounds in the HPV program. Other chemicals in this category are scheduled for review under the ICCA program and are undergoing or have undergone review in the OECD SIDS program. The data from these chemicals provides a more complete understanding of this category, and they are listed in Figure 2.

Figure 1. Ring-substituted Anilines Included in the HPV Program



Chemical Name	CAS Number	R1	R2	R3	R4	Program
2,6 Diethyl Aniline	579-66-8	H	H	C_2H_5	C_2H_5	HPV
Ortho Ethvl Aniline	578-54-I	H	H	C_2H_5	H	Extended HPV

Figure 2. Related Anilines



Chemical Name	CAS Number	R1	R2	R3	R4	Program
2,6 Methyl Ethyl Aniline	24549-06-2	H	H	CH_3	C_2H_5	OECD SIDS
Aniline	62-53-3	H	H	H	H	OECD SIDS

Manufacturing, Use and Exposure Information on Ring-substituted Anilines

2,6-DEA is a representative ring substituted aniline prepared by ot-thoalkylation chemistry. This process involves the reaction of aniline with ethylene catalyzed by aluminum anilide catalyst. The catalyst is prepared by the reaction of aniline with triethylaluminum.

The largest category of use for these chemicals is as chemical intermediates in the synthesis of a variety of organic chemicals. Because the majority of the production volume is converted to other chemicals (i.e., is used as a chemical intermediate), human and environmental exposure to the original chemical is limited. 2,6 Diethyl aniline has been reported to be an intermediate for the manufacture of agriculture products, dyestuffs, antioxidants, pharmaceuticals, synthetic resins, fragrances and other products (Kuney, JH ed, 1992). 2,6 DEA is used in the production of triazine herbicide. (Kirk-Othmer, 1991). OEA has been reported to be used as an intermediate for pharmaceuticals, dyestuffs, pesticides and other products (Lewis, RJ, ed, 1997)

Because of their use as chemical intermediates, the potential for exposure exists primarily in the workplaces of the manufacturers and their customers. The manufacturers use and recommend both personal protective equipment and engineering controls. Splash-proof chemical safety goggles, full-faceshields, or full-face respirators are recommended to protect against eye contact. Local exhaust ventilation is recommended to minimize inhalation exposure. Organic vapor cartridge respirators are recommended for use if there is a potential for exposure to vapors or mists. In case of a spill or leak, appropriate protection, which may include a respirator with supplied air, is required. Appropriate gloves, aprons, and chemical resistant clothing are used to prevent dermal contact.

Test Plan Rationale

There is a large amount of test data available for the sponsored HPV substituted anilines and the other related anilines. These data allow the use of categories and estimation to predict effects where data are missing. The summary documents enclosed for each chemical summarize the available studies. The critical studies to fulfill required HPV Challenge endpoints were chosen according to several factors, including documentation and detail, when the study was conducted, and access to a detailed publication or report. Overall, existing data has been identified for all of the HPV Challenge endpoints.

Physical and Chemical Properties

The physical and chemical properties of all the chemicals in the category are summarized in Table 1 below. All the compounds are liquids at room temperature, with relative densities ranging from 0.967 to 1.02. The boiling points all range from 184°C (aniline) to 241 °C (2,6 DEA). The vapor pressures at 25 °C range from is from 0.0038 mm Hg for 2,6 DEA to an estimated value of 0.49 mm Hg for aniline. The water solubility estimates range from less than 1 g/L for the substituted anilines to 36 g/l for aniline. The range of the log of the octanol-water partition coefficients is from 0.91 (aniline) to the estimate of 3.15 for DEA. These data are sufficient to describe the properties of this category, and no further testing is proposed.

Table 1: Data Values: Physical and Chemical Properties

	Aniline 62-53-3	2,6 Diethyl aniline 579-66-8	2,6 methyl ethyl aniline 24549-06-2	Ortho ethyl aniline 578-54-1
Molecular Weight	93.13	149.24	135.21	121.18
Melting Point (°C)	-6.2	3.5	-33 40.13 (est)	-46.5 22.88 (est)
Boiling Point (°C)	184.0	231 241 (est)	231 at 1013 hPa	209.65 223.43 (est)
Density g/cc at 20°C	1.0213	0.959	0.97	0.98
Vapor Pressure	0.49 mm Hg at 25°C	0.00383 mm Hg at 25°C	0.063to 0.8 hPa at 20°C 0.0742 mmHg (est)	0.17 mmHg at 25°C 0.22 (est)
Log P	0.9 1.08 (est)	0.95 3.15 (est)	2.66 (est)	1.74 2.11 (est)
Water Solubility	36 g/l at 20°C	670 mg/l (est)	2.66 g/l at 22°C 467.3 to 704.86 mg/L at 25°C (est)	416 to 3245 mg/l (est)

(est) – EPIWIN Model Estimate

Metabolism

Metabolism of arylamines generally proceeds through N-oxidation, hydroxylation of aromatic ring carbons, and formation of conjugates such as glucuronides, sulfates, and acetates to expedite elimination (Kharchevnikova and Zholdakova, 1997; Cheever et al, 1980; Son et al, 1980). Ring alkyl substituents may also be oxidized to alcohols and further metabolized to acids (Son et al, 1980). N-Oxidation is an important step that can lead to the formation of metabolites that will react with cellular macromolecules (Kiese, 1963; Burstyn et al, 1991; Garner et al, 1984). The N-phenylhydroxylamines and nitrosobenzenes produced by N-oxidation are capable of binding to the heme ion in hemoglobin and causing oxidation. This reaction can produce the methemoglobinemia that is the most typical toxicity associated with aromatic amines. Aniline itself is oxidized primarily to o- and p-aminophenol. These metabolites are subsequently conjugated with glutathione to form o- and p-aminophenylmercapturic acids for urinary excretion (Radomski, 1979; Baranowska-Dutkiewicz, B, 1982; Irons et al, 1980; Williams, 1959; Parke, 1960).

The most common metabolic reaction for the toluidines is ring hydroxylation. o-Toluidine undergoes hydroxylation in the para position, as well as a lesser amount of N-acetylation, and conjugation with sulfates and glucuronides (Cheever et al, 1980; Son et al, 1980). Ortho ethyl aniline should undergo similar hydroxylation.

Metabolic studies of 2-ethyl 6-methyl aniline in rats, using oral, dermal and inhalation routes showed rapid excretion, primarily by the kidney. The major metabolite in the urine was the sulfate ester conjugate of 2-ethyl-4 hydroxy-6-methyl aniline. It represented 65% (oral, low dose), 77% (oral, high dose), 60% (dermal) and 51% (inhalation) of the dose given. (Hambock, H, 1982 – see 2,6 MEA IUCLID)

Metabolic studies are available for 2,6 DEA. Oral or dietary doses in rats showed that for 2,6 DEA, the urine was also the major metabolic route of elimination. Male rats eliminated 54.6 to 73.6% (Long Evans versus Sprague Dawley rats) in the urine from dietary exposure, and 49-9 to 66.6% after gavage dosing. Female rats after gavage dosing eliminated 70.4% via the urine.

Incubation of 2,6 diethylaniline with NADPH microsomes produced 4-amino-3,5-diethylphenol as the major incubation product. The phenol undergoes further oxidation to 3,5 diethyl-benzoquinone-4-imine, which is isolated as a minor metabolite during 2,6-diethylaniline metabolism (Snyder, R., ed., 1990)

Fate

The data values for environmental aspects are summarized in Table 2 below.

In general, anilines absorb light in the environmental UV spectrum (> 290 nm). Thus, 2,6 DEA is expected to absorb light and may potentially undergo direct photolysis. However, 2,6 DEA is not predicted to partition to the air in significant amounts. Due to the low vapor pressure, the 2,6 DEA that does occur in the ambient atmosphere will be in the vapor phase. Vapor phase 2,6 DEA is predicted to degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be 0.792 hours, calculated from it's rate constant of 1.6 x 1 O-l 0 cu cm/molecule-set at 25°C. OEA, has an estimated half-'life for the same reaction of 0.971 hours.

If released into water, biodegradation is a major removal process for aniline. A short acclimation period generally enhances biodegradation of aniline. Biodegradation has been studied extensively for aniline – it is even used as a reference chemical in ready biodegradation testing to validate the testing system.

However, the substituted anilines can be predicted to not readily biodegrade, using environmental modeling tools. This is demonstrated by biodegradation testing of 2, 6 methyl ethyl aniline, where values of 0 to less than 10% biodegradation has been seen in ready biodegradation tests (OECD 301 D and E).

Based on estimated log Koc values, the substituted anilines would be expected to have slow to moderate migration through soils and low to moderate sorption to soils. However, aromatic amines (including aniline) bind to humic material in two phases (a rapid, equilibrium phase, and a slower, less reversible phase) which could decrease movement in soil. (Parris, GE, 1980).

Adsorption to sediments is predicted to be low for all these aromatic amines, but the protonated forms of these chemicals will bind more strongly. Aniline with a pKa of 4.6 will exist partially in the protonated form in aqueous environment, and the protonated form of aniline is not expected to volatilize from water. In moist soils, the protonated form will bind strongly to soil surfaces. Ortho ethyl aniline has a pKa of 4.3 also will partially exist as the protonated form, which will bind to soil surfaces and not volatilize. 2,6 DEA would react similarly.

None of the ring substituted anilines is likely to bioaccumulate in aquatic organisms, based on the estimated octanol-water partition coefficients. Measured BCF values of less than 10 in fish suggests that bioconcentration of aniline in aquatic organisms is low. Estimated BCF values for the substituted anilines are from 4.4 (OEA) to 53 (DEA). Lack of bioaccumulation has been demonstrated for 2,6 DEA in fish, where the bioconcentration factor was found to be 120.

If released into soil, leaching and reaction with organic constituents are expected to be major removal processes. Binding to soil is predicted to be low to moderate, and as for sediments, binding will vary with pH and humic material. Evaporation from dry soil is expected to be low, because of low estimated vapor pressures.

Degradation in soil systems is also likely. 2,6 DEA is degraded by soil microorganisms such as Chaetomium globosum (Snyder, 1990), and in nonsterile soils, 40-75% of applied DEA can disappear in 20 hours. These transformation rates are affected by pH – increasing transformation with acidity (Bollag, JM, 1987). When tested in an enclosed aquatic system containing planktons, insects and snails, 2,6 DEA was considered readily biodegradable based on the organisms abilities to quickly eliminate it (Lu, PY, 1974).

There are sufficient data for these substituted anilines to characterize the fate of these chemicals. None of the substituted anilines meet the criteria for Persistent, Bioaccumulative and Toxic (PBT) chemicals, and no further testing is proposed.

Aquatic Toxicity

In most acute toxicity tests, the 2,6 DEA and the related compounds were harmful to fish (96-hr LC50 values >10 mg/L <100 mg/L. Experimental data was available for several fish species for 2,6 DEA (24-30 mg/l 96 hour LC50 values), and estimated for OEA (30.2 mg/L).

Ring substituted anilines in the category were harmful to algae (similar to aniline), or not tested. 2,6 DEA has not been tested, but is predicted to be similar to MEA (58 mg/L over 5 days) and OEA (38 mg/L).

Invertebrate toxicity values range from 0.25-3 mg/l LC50 at 48 hours for aniline to 21 mg/l (DEA). MEA and OEA have also been tested in Daphnia, with LC50 values of 12.8 to 13.5 for MEA and 8.05 for OEA.

There is a large amount of aquatic toxicity data available on chemicals in this category, and no further testing is proposed.

Table 2: Data Values: Environmental Aspects

	Aniline 62-53-3	2,6 Diethyl aniline 579-66-8	2,6 methyl ethyl aniline 24549-06-2	Ortho ethyl aniline 578-54-1
Environmental Fate				
Photodegradation	Air partitioning likely low	Air partitioning likely low	Air partitioning likely low	Air partitioning likely low
Indirect photolysis, rate constant cm^3/ (molecule * sec)	1.1 - 1.18 x 10^{-10} (measured)	1.62 x 10^{-10} (estimated)	1.62 x 10^{-10} (estimated)	1.32 x 10^{-10} (estimated)
Hydrolysis	11.3% (pH 6, 30'C) after 48 hours	Lacks functional groups likely to hydrolyze	Lacks functional groups likely to hydrolyze	Lacks functional groups likely to hydrolyze
Distribution (PBT profiler)	Air: 0% Water: 45% Soil: 54% Sediment: 0%	Air: 0% Water: 19% Soil: 80% Sediment: 1 %	Air: 0% Water: 22% Soil: 78% Sediment: 0%	Air: 0% Water: 37% Soil: 63% Sediment: 0%
Biodegradation % biodegradation/days	92-97%/ 6 days	Not expected to readily degrade	0-10%/ 28 days	Not expected to readily degrade
Log Koc	1.65 (est)	2.659 (est)	2.374 (est)	2.155 (est)
Ecotoxicity				
Acute fish LC50, 96 hours	ca 10 ppm	30.2 (est)	13.2 (est)	30.2 (est)
Winter flounder	--	29 mg/l	35 mg/l	--
Trout	8.2 mg/l a	24 mg/l	43-1-44 mg/l	--
Bluegill	--	30 mg/l	--	--
Acute invertebrate LC50, 48 hours	0.25-0.3 mg/l	21 mg/l	12.8-13.5 mg/l	8.05 mg/l
Acute algal, EC50	19 mg/l 96 hr 94-175 mg/l 72 hr	--	58 mg/l (5 days)	38 mg/l
Bioaccumulation: BCF Estimated or experimental	2.6 (exp)	53 (est) 120 (exp)	22 (est)	4.4 (est)

a Abram, et al, 1982.

Mammalian Acute Toxicity

The data values for toxicity are summarized in Table 3 below. The ring substituted anilines have been tested for acute toxicity. All can be considered harmful by single oral doses, as the rat oral LD50's are generally >500 to > 2000 mg/kg. There is a single oral LD50 value for 2, 6 DEA of 2690 mg/kg. increasing alkyl substitution on aniline appears to lessen the acute oral toxicity.

In a study of the effect of substituents on acute rat toxicity in mono- and di-alkyl ring substituted derivatives of aniline, Jacobson (1972) found that the alkyl substituted anilines were less acutely toxic than aniline, and that length of chain (Cl to C3) on a single e-substituted aniline does not change toxicity, but that toxicity decreases with increasing chain length on the 2,6 disubstituted anilines.

Comparison of LD50 and Substituent Group of Aniline Derivatives

	LD50 (g/kg)	
Alkyl group	2-alkyl	2,6 dialkyl
Methyl	0.90	0.84
Ethyl	1.26	2.69
Isopropyl	1.18	4.27

The rabbit dermal LD50's for the disubstituted compounds are > 1000 mg/kg by single dermal applications. Ortho ethyl aniline had a dermal LD50 value of 840 mg/kg, more like aniline (820 mg/kg and lower values reported) Where systemic toxicity was found, all these compounds caused cyanosis and increased respiratory rate from methemoglobinemia. These material are irritant to they eyes, and can cause irritation of the skin. No further testing is proposed for the ring substituted anilines for acute toxicity.

Mammalian Repeated Dose Toxicity

Oral or inhalation repeated exposure studies have been completed on 2,6 DEA, aniline, and 2,6 MEA. In a direct comparison, aniline, o-toluidine, 2,6 DEA, and 2,6 MEA and other anilines were given orally to rats for 5, 10, or 20 days at one-fourth of the LD50. Histopathology examinations found splenic congestion, increased hematopoiesis, hemosiderosis, and periacinar vaculolar changes in all. (Short et al, 1983).

2,6 DEA has been tested by repeated dose exposure by oral, dermal, inhalation and dietary routes, and has included rat, dog, and rabbit species. Studies have ranged in length from 28 day, to 90 day to lifetime chronic toxicity studies.

Based on the length of studies, the multiple routes and species, as well as consistent acute results for all the compounds, no further repeated exposure testing is proposed.

Genetic Toxicity

Standard bacterial mutagenicity assays with and without metabolic activation have been conducted for aniline and the ring substituted anilines considered. Aniline has shown positive results in some Ames tests. 2,6 DEA, 2,6 MEA and OEA, for the most part, have negative Ames test results. 2,6 DEA and 2,6 MEA showed weak positive reactions in tester strains T98 and T1 00 with activation. In these cases, increase in revertants in those strains were no more than twice that of negative controls.

In Vivo, 2,6 DEA and 2,6 MEA did not induce micronuclei in the mouse micronucleus assay. Aniline was negative in a dominant lethal assay.

No further testing is proposed for genetic toxicity for this group.

Table 3: Data Values: Toxicity

Mammalian Toxicity				
Acute toxicity: Oral, rat, LD50	440-750 mg/kg	2690 mg/kg 1800 mg/kg	885, 1180, 1150, 1200 mg/kg	1260 mg/kg
Dermal, rabbit, LD50	820-1540 mg/kg	1100 mg/kg	1290 mg/kg	840 mg/kg
Inhalation, rat, LC50 4 hours	550 ppm	> 33 ppm	> 260 ppm	> 65 ppm (1-4 hours)
Skin irritation	Mild	Moderate	Not irritating	Not irritating
Eye Irritation	Irritant	Irritant	Irritant	Irritant
Repeated dose toxicity Oral route, length	20 day	20 day	20 day	C
Dietary route, length	24 months	28 and 90 day		
Dermal route, length		28 day		
Inhalation route, length	14 days	30and 90day		
Genetic toxicity				
in vitro: gene mutation Bacteria: Ames test	Positive	Negative most T weak +T98T100	Negative (two) weak +T98,T100 in one test	Negative
in vitro: chromosome aberrations Cytogenetics, CHO or CHL	Weak + with activation			Negative
in vitro: cell transformation				C
SHE cells	Negative			
BALB3/C3 cells	Positive	Negative	Negative	
in vivo:				C
Micronucleus	Most Positive	Negative	Negative (two)	
Cytogenetics, rodent	Negative	Negative		
Dominant Lethal, rat				
Carcinogenicity				
Rat	+ Spleen	Negative	C	C
Mouse	Negative			
Reproductive toxicity	P	P	C	C
Developmental toxicity	Negative, rat	Negative, rat	C	C

C = Use of Category Approach
P = >90 Day study found no pathology of reproductive organs

Developmental and Reproductive Toxicity

A full developmental toxicity study in rats for 2,6 DEA found fetotoxicity at maternally toxic doses, but no evidence of teratogenicity or embryotoxicity. Other compounds in the category have also been tested for developmental toxicity. A full developmental toxicity study of aniline failed to find evidence of a teratogenic effect.

Consideration is given to effects on reproductive organs in repeated exposure studies to determine whether further reproductive toxicity studies are needed. 2,6 DEA was tested in repeated dose studies ranging from 28 days (dietary and dermal routes), 90 days (dietary and inhalation), and 24 months (dietary) in length. Subchronic and chronic studies of aniline in rats and mice found no evidence that reproductive organs would be affected.

A dominant lethal study of aniline in rats was also completed to address the possibility of heritable effects being transmitted to the offspring from parental males. No dominant lethal effect was found in the rat. In keeping with the lack of heritable genetic damage from aniline exposure.

As the substituted anilines are covered by the subchronic, chronic, and developmental data discussed above for these and related aromatic amines, no further testing for reproductive toxicity is proposed.

The existing data summary and proposed test plan are summarized in Table 4 below.

Table 4. Summary of Data Gaps and Method of Completion

	Aniline 62-53-3	2,6 Diethyl aniline 579-66-8	2,6 methyl ethyl aniline 24549-06-2	Ortho ethyl aniline 578-54-1
Environmental Fate				
Photodegradation	A	S	S	S
Hydrolysis	A	C	C	C
Fugacity	S	S	S	S
Biodegradation	A	S	A	S
Ecotoxicity				
Acute fish	A	A	A	S
Acute invertebrate	A	A	A	A
Acute algal	A	C, S	A	A
Mammalian Toxicity				
Acute toxicity	A	A	A	A
Repeated dose toxicity	A	A	A	C
Genetic toxicity				
in vitro: gene mutation	A	A	A	A
in vitro: chromosome aberrations	A	A	A	C
in vitro: cell transformation	A	A	A	C
in vivo: chromosome aberrations	A	A	A	C
Reproductive toxicity	P	P	C	C
Developmental toxicity	A	A	C	C

= ICCA and OECD SIDS chemicals (testing will be addressed under ICCA HPV Program)

A = Adequate data available
T = Testing to be done
NG=Non-guideline data available
S = Structure-activity relationship (modeling program used)
C = Use of Category Approach
P = >90 Day study found no pathology of reproductive organs

Aniline Category References:

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Short, C.R., King, C., Sistrunk, P.W., and Kerr, K.M., Subacute Toxicity of Several Ring-Substituted Dialkylanilines in the Rat, Fundamental. Applied Toxicology,.Vol. 3, No. 4, 285-292,1983.

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Son, O.S., Everett, D.W., and Fiala, E.S.,"Metabolism of o-[methyl-^{14}C]toluidine in the F344 rat", Xenobiotica, 10, 457-468, 1980.

Williams, R.T., Detoxification Mechanisms, 2nd ed., London, Chapman and Hall Ltd., pp. 430-432, 464-465 (1959); in "IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Some Aromatic Amines, Anthraquinones and Nitroso Compounds, and Inorganic Thiorides Used in Drinking Water and Dental Preparations", Lyon, France. 27, 39-61 (1982).

D a t a S e t

Existing Chemical	Substance ID: 62-53-3
CAS NO.	62-53-3
EINECS Name	aniline
EINECS No.	200-539-3
TSCA Name	Benzeneamine
Molecular Weight	93.13
Molecular Formula	C6H7N

2. Physico-chemical Data

2.1 Melting Point

Value: -6.2°C
Reference: BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

2.2 Boiling Point

Value: 184.0°C
Reliability: (1) valid without restriction
Flag: robust summary
Reference: BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

2.3 Density

Type: relative density
Value: 1.0213 at 20°C
Reliability: (1) valid without restriction
Flag: robust summary
Reference: BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

2.4 Vapour Pressure

Value: 0.49 mm
Temperature: 25°C
Method: calculated[I; measured [x]

GLP: Yes[I No[ ] ?[ ]
Remarks:
Reference: Danner, R.P., Physical and Thermodynamic Properties of Pure Chemicals, Design Inst. Phys. Prop. Data. Amer. Inst. Chem. Eng. NY; NY: Hemisphere Pub. Corp. Vol. 4 (1989); Daubert, T.C. and Danner, R.P., (1985), in EPISUITE v. 3.10, physical properties of aniline.

2'5 Partition Coefficient

log Pow: 0.91
Method:
Year:

Reference: BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

2.6.1 Water Solubility

Value: 36 g/l at 20°C
pH: 8.8 at 36 g/l and 20°C
Reference: BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

3.1.1 Photodegradation
Type : Air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Rate constant: • sec)
Method Measured
Year: GLP: no
Test Substance:
Remark: Concentration of sensitizer: about 10e10 molecule/cm3
Tropospheric halt-lifetime 3.5 h calculated from the measured degradation constant, assuming a tropospheric OH radical concentration of 5 x 10e5 radicals/ml
Test condition: Absolute rate technique. OH radicals are monitored as a function of time after the pulsed flash lamp by resonance fluorescense detection system (RF)
Reference: Witte, F. et al. J. Phys. Chem. 90, 3251-3259 (1986).

Type: Air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Rate constant: . 000000000118 cm3/(molecule • sec)
Method Measured
Year: GLP: no
Test Substance:
Remark: Concentration of sensitizer: 10e11 10e13 molecule/cm3
Tropospheric half-lifetime 3.26 h calculated from the measured degradation constant, assuming a tropospheric OH radical concentration of 5 x 10e5 radicals/ml
Test condition: Absolute rate technique, OH radicals are monitored as a function of time after the pulsed flash lamp by resonance fluorescense detection system (RF)
Reference: Atkinson, R., Chem. Rev. 85. 69-201 (1985).

3.1.2 Stability in Water
Type : Abiotic (hydrolysis) [x]; biotic (sediment) [ ]
Degradation: 11.3+9.9% at pH approx. 6.0 at 30°C after 48 hours
Method: Schultz, T.W. et al, Bull. Environ. Toxicol. Chem. 42. 192-198 (1989);Yoshioka, Y. et al, Sci. Total Environ. 43, 149-157 (1985).

GLP: Yes[ ] No[x] ?[ ]
Remarks: Concentration tested was 71 mg/L.
Reference: Arnold, L.M. et al, Chemosphere 183-191 (1990).

3.5 Biodegradation

Type: aerobic
Inoculum: BASF-activated sludge
Concentration: 596 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: 97 % after 5 days
Method: Modified OECD Screening Test
Year: GLP: no
Test substance: no data
Reference: EASF AG, Ecology Laboratory, unpublished research: Biotic Degradation: Modified OECD Screening Test of 6/5/81.

Type: aerobic
Inoculum: BASF-activated sludge
Concentration: 100 mg/l related to WC (Dissolved Organic Carbon)
Degradation: 92 % after 6 days
91% after 3 days
39% after 1 day
15% after 3 hours
Method: Standard experimental method
Year: 1980 GLP: no
Test substance: no data
Reference: BASF AG, Ecology Laboratory, unpublished research: Biotic Degradation: Standard experimental method of 5/6/80.

3.7 Bioaccumulation

Species: Brachydanio rerio (fish, fresh water); static
Exposure period: 24 hours
Concentration: 2 µg/l
BCF: 2.6 ± 0.27
3LP: No data
Remark: Uptake constant was 11.1 ± 3.2/h. Aniline concentrations were measured via HPLC.
Reference: Zok, S.. Sci. Total Environ. 109/110, 411-421 (1991).

Species: (Algae)
Exposure period: 24 hours
Concentration: 0.36 mg/l and 2 mg/l
BCF: 9:
GLP: No data
Reference: Hardy. J.T. et al., Environ. Toxicol. Chem. 4, 29-35 (1985).

4.0 Ecotoxiciry

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)

Unit:	mg/l	Analytical monitoring:
EC50:	.25	
Method:	Plow-through	
Year:		GLP: no data
Test substance:		
Test condition:	17.2 degrees	7.4
Reference:	Holcombe, G.W. et al., Arch. Environ. Contam Toxicol. 16, 697-710 (1987).	

species:	Daphnio magna (Crustacea)	
Exposure period:		
Unit:	mg/l	Analytical monitoring:
EC0:	.01	
EC50:	.3	
EC100:	1.2	
Method:	Daphnia Short Term Test, DIN 38412 Part 11, Determination of the Effect of Substances in Water on Crustacea	
Year:		GLP: no
Test substance:		
Reference:	Kuehn, R. et al., Research report: Harmful effects of environmental chemicals in the Daphnia Reproduction Test *as* a basis *for* the *verification of* environmental hazards in aquatic systems (UFOPLAN Nr. 1063052). Berlin (1988).	

4.3 Toxicity to Aquatic Plants e.g. Algae

Species:		(Algae)
Endpoint:	growth rate	
Exposure period:	72 hours	
Unit:	mg/l	Analytical monitoring: yes
EC50:	94-175	
Method:	OECD Guide-line 201 "Algae, Growth Inhibitioo Test"	
Year:	1984	GLP: no data
Test substance:	purity: 99.5% (Merck, Darmstadt, Germany!	
Reference:	Ramos, E.U. et al, Aquatic Toxicology 46, 1-10 (1999).	

Species:		(Algae)
Kndpoint:	growth rate	
Exposure period:	96 hours	
Unit:	mg/l	Analytical monitoring:
EC50:	19	
Method:	EPA algal growth inhibition test	
Year:	1971	GLP: no
Test substance:		
Reference:	Calamari, D. et al., Chemisphere 9, 753-762 (1980).	

5. Toxicity

5.4 Repeated Dose Toxicity

Species:	rat	Sex: male
Strain:	Fischer 344	

Route of admin.:	oral gavage; no vehicle
Exposure period:	5, 10, or 20 Days
Frequency of treatment:	daily
Post. obs. period:	none
Dose:	110 mg/kg body weight per day
Control Group:	yes; sham dosed
Method:	Described in the publication
Year:	GLP: no data
Test substance:	99.9% purity (MCB Chemicals)
Result:	Deaths. decreased body weights/S days) and increased spleen weights; transient cyanosis after dosing; rough hair coat; splenic congestion, increased hematopoiesis and hemosiderosis, and bone marrow hyperplasia.
comments :	Blood changes were consistent with enhanced
Reference:	Short, C.R. et al. Fundam. Appl. Toxicol. 3, 285-292 (1983).

Species:	rat sex: male
strain:	NC data
Route? of admin.:	inhalation
Exposure period:	2 weeks
Frequency of treatment:	3, 6, or 12 hr/day, 5 days/week
Post. obs. period:	14 days
Doses:	0, 10, 30. or 90 ppm
Control Group:	yes
NOAEL:	10 ppm
Test substance:	
Result:	At ≥ 30 ppm: concentration dependent effects, splenic congestion, hemolysis, increased MCV, MCHb and methemoglobin values; methemoglobin values were normal within 14 days after exposure. and spleen values were nearly normal.
Comments:	Concentration. not time. was the primary determinant to use in setting exposure limits
Reference:	Burgess, B.A. et al., The Toxicologist 4. p. 64 [A] (1984).

5.5 Genetic Toxicity 'in Vitro'

Type:	Cytogenetic assay
system of testing:	Chinese hamster lung (CHL) fibrcblast cells
concentration:	1000 ug/ml
Metabolic activation:	with and without
Result:	positive with activation at 1000 ug/ml and higher
Method:	Ishidate Jr.. M. (Ed.! (1987) Chromosomal Aberration Test in Vitro, L.I.C.. Inc.. Tokyo.
Year:	GLP: no data
Test substance:	

Reference:	Ishidate,Jr., M., et al., (1988): Mutat. Res. 195, 151-213.
Type:	Cytogenetic assay
system of testing:	Chinese hamster (v79) cells
Concentration:	
Metabolic activation:	with and without
Result:	positive
Method.	
Year:	GLP: no data
Test substance:	
Reference:	Miltenburger, H.G., Test report of study LMP 102. Laboratory for mutagenicity resting, Technical University Darmstadt (1986); on behalf of BG Chemie, Heidelberg.
Type:	Cytogenetic assay
system of testing:	Chinese hamster ovary (CHO) cells
Concentration:	160 to 1600 ug/ml without activation; 500 to 5000 ug/ml with activation
Metabolic activation:	with and without
Result:	weak positive with activation at 5000 ug/ml only
Method:	Gallowav at al (1985)
Year:	GLP: no data
Test substance:	obtained from NTP chemical repository
Reference:	Galloway, S.M. et al, Environ. Mol. Mutagen. 10 (Suppl. 10), l-175 (19871.
Type :	Cell transformation
System of testing:	Balb/3T3
Concentration:	0.8, 4, 20, and
Metabolic activation:	none
Result:	positive
Method:	Kakunaga, T., Int. J. Cancer 12, 463-473 (1973).
Year:	GLP: no data
Test substance:	supplied by the NCI Chemical Repository
Reference:	Dunkel, V.C. et al. J. Nat. Cancer Inst. 67(6), 1303-1315 (1981).
Type :	Cell transformation
system of testing:	SHE
Concentration:	0.05. 0.50, and 5.0 ug/ml
Metabolic activation:	none
Result:	**negative**
Method:	Freeman. A.E. et al, J. Nat. Cancer Inst.51, 799-808 (1973); Pienta, R.J. et al, in: Nieburgs HE, et al, eds.. Cancer Prevention and Detection. Pert I. Vol 2

New York: Marcel Dekker, 1978:1993-2011; DiPaolo, J.A. et al, Cancer Res. 31, 1118-1127 (1971).

Year: GLP: no data
Test substance: applied by the NCI Chemical Repository
Reference: Dunkel, V.C. et al, J. Nat. Cancer Inst. 67(6), 1303-1315 (1981).

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: mouse Sex: male and female
strain: SJL Swiss
Route of admin.: intraperitoneal
Exposure period: single administration; animals killed after 24 hr
Doses: 0, 5, 50, 100. and 200 mg/kg bw
Method: no data; method described in publication
Year: GLP: no data
Teat substance: Purified by recrystallization or distillation
Result: positive
Reference: Sicardi, S.M., et al., J. Pharm. Sci. 80(8), 761-764 (1991).

Type : Cytogenetic assay
Species: mouse Sex: male
Strain: CRH
Route of admin.: oral.
Exposure period: single administration; animals killed after 24 and 48 hr
Doses: 0, 400, 500, and 1000 mg/kg bw
Method: giver. in publication
Year: GLP: no data
Test substance: hydrochloride salt, purity >99%
Result: positive at 1000 mg/kg
Reference: Westmoreland, C. and Gatehouse, D.G.. Carcinogenesis 12(6), 1057-105s (1991).

Type : Cytogenetic assay
Species: rat sex: male
Strain: PVG
Route of admin.: oral gavage
Exposure period: single administration;animals killed after 24 and 48 hr
Doses: 0, 215, 287. 400, and 500 mg/kg body weight
Method: Schmid, W., Mutat. Res. 31, 9-15 (1975).
Year: GLP: no data
Test substance: hydrochloride salt
Result: Positive
Reference: George, E. et al.,Carcinogenesis 11(9), 1551-1555 (1990).

Type: Cytogenetic assay
Species: mouse sex: male
strain: CBA
Route of admin.: intraperitoneal
Exposure period: two injections 24 hr apart; animals killed after 24 and 48 hr

Doses	experiment 1: 0,100, 200, 250, and 300 mg/kg body weight Experiment 2: 0, 237.5, and 380 mg/kg body weight
Method:	Schmid, W., Mutat. Res. 31. 9-15 (1975)
Year:	GLP: no data
Test substance:	AnalaR grade material used: redistilled
Result:	Positive
Reference:	Ashby, J., et al.. Mutat. Res. 263, 115-117 (1991).

Type:	Dominant lethal assay
Species:	rat
Strain:	Alpk:ApfSD (Wistar-derived)
Route of admin.:	intraperitoneal
Exposure period:	5 consecutive days
Doses:	0, 75, 155, 200 mg/kg body weight
Result:	No evidence of a dominant lethal effect
Method:	OECD Guideline 478 'Genetic Toxicology: Rodent Dominant Lethal Test'
Year:	1598 GLPL yes
Test substance:	purity 99.9%
Remark:	methyl (MMS) used as positive clearly positive
Reference:	Milburn, G.M. Central Toxicology Laboratory report no. CTL/P/5404: Aniline: Dominant Lethal Study in the Rat, 4/17/98 (at the request of the Aniline Association Inc.)

5.7 Carcinogenicicy

Species:	rat Sex: male and female
Strain:	F344
Route of admin.:	oral feed
Exposure period:	104 weeks
Frequency of Treatment:	daily
Post. Obs. Period:	none
Doses:	0, 100 mg/kg body weight
Control Group:	yes
Method:	
Year:	GLP:
Test substance:	hydrochloride salt
Result:	Decreased mean hematocrit, hemoglobin, and erythrocytes in mid- and high-dose males and high-dose females. Increased absolute/relative spleen weights in mid- and hiqh-dose males and females. Strcmal hyperplasia and fibrosis of the splenic red pulp in high-dose melas and, to a lesser degree, in females. Chronic capsulitis in high-dose animals. Increased incidence of primary splenic sarcomas principally in high dose males (males: 0, 0, 1.3, and 37.8%: females: 0. 0. 0, and 1.3%).
Reference:	Anon.. 104-Week chronic toxicity study in rats. aniline hydrochloride. CIIT, Research Triangle Park, USA (1982); Bus, J.S., and Popp, J.A., Fd. Chem. Toxicol. 25(8), 619-626 (1987).

Species:	rat Sex: male and female
Strain:	F344
Routs of admin.:	oral feed
Exposure period:	103 weeks
Frequency of Treatment:	daily
Post. Obs. Period:	low dose 4 weeks; high dose 5 weeks; control 7 weeks
Doses:	0, 3000, or 6000 ppm in diet
Control Group:	yes
Method:	
Year:	GLP:
Test substance:	hydrochloride salt
Result:	17/25, 34/50 and 27/50 males and 16/25, 44/50 and 41/50 females survived on test until the end of the study. Slight mean body weight depression ix? treated females and high-dose males. Increased incidence of splenic or abdominal fibrosarcomas and sarcomas. The incidence of combined sarcomas and fibrosarcomas was 0/25, 5/50 and 18/48 in males and 0/24, 1/50 and 7/50 in females. Splenic hemangiosarcomas were significantly increased in males (0/25, 19/50 and 21/48).
Reference:	Anon., Bioassay of aniline hydrochloride for possible carcinogenicity, CAS No. 142-04-l. technical report series no. 130 (NTIS PB-287539). Nat. Cancer Inst., Bethesda. 67

Species:	mouse Sex: male and female
Strain:	B6C3F1
Route of admin.:	oral feed
Exposure period:	103 weeks
Frequency of Treatment:	daily
Post. Obs. Period:	low and high dose 4 weeks; control 6 weeks
Doses:	0, 6000, or 12000 ppm in diet
Method:	yes
Year:	GLP:
Test substance:	hydrochloride salt
Result:	33/50, 43/50, and 41/50 males and 30/50, 37/50, and 41/49 females survived on test until the end of the study. Mean body weight depression in dosed males. No increased incidence of tumors was observed in males or females when compared with control animals.
Reference:	Anon., Bioassay of aniline hydrochloride for possible carcinogenicity. CAS No. 142-04-l. technical report series no. 130 (NTIS PB-287539). Nat. Cancer Inst., Bethesda, 67

5.9 Developmental Toxicity/Teratogenicity

Species :	rat Sex: female
Strain:	F344
Route of admin.:	oral gavage
Exposure period:	days 7-20 of gestation

Frequency of treatment:	once per day
Doses:	0, 10, 30, or 100 mg/kg body weight
Method:	yes
Year:	given in publication
Test substance:	GLP: yes
Remark:	hydrochloride salt: Eastman Kodak Cc.
Result:	minimum of 20 rats/dose group.
	dams: ≥10 mg/kg: dose-dependent increase in relative spleen weights
	dams: 100 mg/kg: significant increases in methemoglobin and hematopoietic activity
	fetuses: 100 mg/kg: increased relative liver weights and hematopoietic activity
Reference:	Price, C.J. et al, Toxicol. Appl. Pharmaccl. 465-478 (1985).

Species:	rat Sex: female
strain:	F344
Route of admin.:	oral gavage
Exposure period:	gestation day 7 through parturition
Post-exposure obs. period:	Pup development was followed from birth to postnatal day 60
Frequency of treatment:	once per day
Doses:	0, 10, 30, or 100 mg/kg body weight
Control Group:	yes
Method:	given in publication
Year:	GLP: yes
Test substance:	hydrochloride salt; Eastman Kodak Cc.
Remark:	15-16 litters/treatment group.
Result:	damn (killed on postnatal day 30): 100 mg/kg: significant increase in relative spleen weights, methemoglobin, and red blood cell size
	fetuses: ≥10 mg/kg: dose-related increase in postnatal deaths
	fetuses: ≤ 30 mg/kg: increased relative liver weights
fetuses: 100 mg/kg:	significant increase in red blood cell size: reduced body weights
Reference:	Price, C.J. et al, Toxicol. Appl. (1985).

IUCLID

Data Set

Existing Chemical ID:	
Memo	
CAS No.	**579-66-8**
EC No.	**209-445-7**
EINECS Name	2,6-Diethylaniline
CAS Name	Benzeneamine, 2,6-diethyl
Common name	2,6 DEA
Molecular Formula	$C_{10}H_{15}N$

Producer related part

Company	Albemarle Corporation
Creation date	

Substance related part

Company	Albemarle Corporation
Creation date	
Status	
Memo	
Printing date	
Revision date	
Date of last update	
Number of pages	
Chapter (profile)	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	: other: sole-representative notifier
Name	:
Contact person	:
Date	:
Street	:
Town	:
Country	:
Phone	:
Telefax	:
Telex	:
Cedex	:
Email	:
Homepage	:

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	: Manufacturer
Name of plant	: Albemarle
Street	:
Town	:
Country	:
Phone	:
Telefax	:
Telex	:
Cedex	:
Email	:
Homepage	:

04.15.2006

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

Remark : The read across of data from compounds of similar chemical structure for the purpose of safety evaluation is not a new concept. Data on several identical endpoints are provided in this dossier for different ring substituted anilines (aniline, 2,6 DEA, 2 methyl 6 ethyl aniline, ortho ethyl aniline) The data show the similarity of toxicological and ecotoxicological properties of these substances. Therefore, it is considered scientifically acceptable to read across data on short-term toxicity and ecotoxicity studies and local effects to other aniline substances without particular tests available. For tests involving the use of experimental animals the read across of data is further supported by animal welfare reasons.

The category approach has already been used for N-substituted anilines by the American Chemical Council Mono Aromatic Amines and Nitroaromatics panel.

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1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name :
Smiles Code : clccc(CC)c(N)cl(CC)
Molecular formula : $C_{10}H_{15}N$
Molecular weight : 149.24 (Lide, DR, ed, 1999)
Petrol class :

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : Typical for marketed substance
Substance type : Organic
Physical status :
Purity : = > 98 % w/w
Colour :
Odour :

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1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Remark : CAS name

Benzeneamine, 2,6-diethyl-

Remark : 2,6-Diethylaniline

2,6-Diethyl aniline

Remark Aniline, 2,6-diethyl

Remark 2,6-Diethylbenzeneamine

Remark : Aniline, 2,6-diethyl

2,6-Diethylphenylamine

Remark 2,6-Diethylbenzamine

Remark : Trade name

DEA

Remark : Trade name

Diethylaniline, 2,6 (DEA)

Remark : Trade name

2,6-DEA

Remark : Trade name

Diethylaniline

1.3 IMPURITIES

04.15.2006

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling : Annex 1 #
Specific limits : No
Symbols : Xn
Nota
R-Phrases : (22) Harmful
S-Phrases : (26) In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
(26) After contact with skin, wash immediately with plenty of . . .
(36/37/39) Wear suitable protective clothing, gloves and eye/face protection
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)

Remark :
04.15.2006

1.6.2 CLASSIFICATION

Classified : Annex 1
Class of danger : Harmful
R-Phrases : (22) Harmful
Specific limits : No
1st Concentration :
2nd Concentration :
3rd Concentration :
4th Concentration :
5th Concentration :
6th Concentration :

7th Concentration :
8th Concentration :
1st Classification :
2nd Classification :
3rd Classification :
4th Classification :
5th Classification :
6th Classification :
7th Classification :
8th Classification :

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1.6.3 PACKAGING

1.7 USE PATTERN

2,6-DEA is used as an intermediate in synthesis of agricultural herbicides. It has been reported as an intermediate for dyestuffs, antioxidants, pharmaceuticals, synthetic resins, fragrances and other products, (Kuney, J.H., ed,. 1992)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

2,6-DEA is prepared by orthoalkylation chemistry. This involves the reaction of aniline with ethylene catalyzed by aluminum anilide catalyst. The catalyst is prepared by the reaction of aniline with triethylaluminum. The reaction is carried out at 300'C under 1000 psi ethylene pressure. The reaction mixture is purified by distillation to give 2,6-DEA which is at least 98% pure.

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Type		Melting Point
Value	: =	3.5°C
Sublimation		
Method		
Year		
GLP		
Test substance	:	as prescribed by 1 .1 • 1.4
Remark	:	Literature value (Daubert, TE, 1989)
04.15.2006		

Type		Melting Point
Value	: =	64.02%
Sublimation		
Method		
Year		
GLP		
Test substance	:	as prescribed by 1 .1 • 1.4
Remark	:	Estimated by MPBPWIN (v1.41) in EPIWIN (v3.12)
04.15.2006		

2.2 BOILING POINT

Type	:	Boiling Point
Value	:	= 242°C at 760 mmHg / 235.5%
Method		
Year		
GLP		
Test substance	:	as prescribed by 1 .1 • 1.4
Remark	:	Albemarle MSDS / Literature value (Dauber-t, TE, 1989)
04.15.2006		

Type	:	Boiling point
Value	: =	259.25%
Method		
Year		
GLP		
Test substance	:	as prescribed by 1 .1 • 1.4
Remark	:	Estimated by MPBPWIN (v1.41) in EPIWIN (v3.12)
04.15.2006		

2.3 DENSITY

Type	:	Density
Value	:	= . 0.96 kg/l @ 20°C
Method		
Year		
GLP		

Test substance : as prescribed by 1.1 - 1.4

Remark : Literature Value (Ashford, RD, 1994)
04.15.2006

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Type : Vapor pressure
Value : = 2.7 Pa at 20°C / 3.83 x 1 0^{-3} mmHg @25°C
Method :
Year :
GLP :
Test substance : as prescribed by 1 .1 - 1.4

Remark : Albemarle MSDS / Literature value (Daubert, TE,1989)
04.15.2006

Type : Vapor pressure
Value : = 0.0587 mmHg at 25°C
Method : Mean of Antoine and Grain methods
Year :
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : Estimated from EPIWIN (v. 3.12)
04.15.2006

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : 0.95
pH value :
Method :
Year : 1975 ,
GLP : no data
Test substance : as prescribed by 1 .1 - 1.4

Remark : Literature Value (Lu, PY, 1975)
04.15.2006

Partition coefficient : octanol-water
Log pow : 3.15
pH value :
Method :
Year : 2006
GLP :
Test substance : as prescribed by 1.1 - 1.4

Remark : Estimated by Log Kow (version 1.67) from EpiWin (v. 3.12)
04.15.2006

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 0.12% weight at 20 670 mg/l @ 26.7°C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other:
Year	:	
GLP	:	
Test substance	:	as prescribed by 1 .1 - 1.4

Remark : Albemarle MSDS / Literature Reference (Yalkowsky, SH, 1992)
04.15.2006

Solubility in	:	Water
Value	:	= 225.92 mg/L
pH value	:	
concentration	:	at 25 °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Estimated by WATERNT program (v. 1 .01) from EPIWIN (v. 3.12)
04.15.2006

2.6.2 SURFACE TENSION

Type	:	Surface Tension
Value	:	= 3.27 x 10-2 N/m
Method	:	
Year	:	
GLP	:	
Test substance	:	as prescribed by 1 .1 - 1.4

Remark : Literature Value (Daubert, TE,.1989)
04.15.2006

2.7 FLASH POINT

Type : Flash Point

Value	: **= 109°C**
Method	: other: TCC
Year	:
GLP	:
Test substance	: As prescribed by 1.1 - 1.4
Remark	: Albemarle MSDS 04.15.2006

2.8 AUTO FLAMMABILITY

2.9 **FLAMMABILITY**

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1 .1 PHOTODEGRADATION

Type	:	Photodegradation
Light source	:	
Light spectrum	:	
Relative intensity	:	
Conc. of substance	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
lest substance		

Remark : In general, anilines absorb light in the environmental UV spectrum (> 290 nm). Thus, 2,6 DEA is expected to absorb light and may potentially undergo direct photolysis. However, 2,6 DEA is not predicted to partition to the air in significant amounts. Due to the low vapor pressure, the 2,6 DEA that does occur in the ambient atmosphere will be in the vapor phase. Vapor phase 2,6 DEA is predicted to degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be 0.792 hours, calculated from it's rate constant of 1.6 x 1 O-1 0 cu cm/molecule-set at 25'C.

Remark : Estimated by AOP program (v. 1.91) from EPIWIN (v. 3.12)
14.02.2002

3.1.2 STABILITY IN WATER

Type	:	Abiotic
	:	
	:	
t1/2 pH9	:	
5	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	

Remark : 2,6 DEA is not expected to undergo hydrolysis in the environment due to lack of hydrolyzable functional groups. (Lyman, WJ, et al. 1990)

Test substance :
04.15.2006

3.1.3 STABILITY IN SOIL

Type	:	
	:	
	:	
	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	

Remark : When incubated with autoclaved soil in a water slurry, 2,6 DEA disappears slowly with about 20% lost in 4 days. However, degradation in natural

soil/water systems is likely. 2,6 DEA is degraded by soil microganisms such as Chaetomium globosum (Snyder, 1990), and in nonsterile soils, 40-75% of applied DEA can disappear in 20 hours. These transformation rates are affected by pH - increasing transformation with acidity (Bollag, JM, 1967).

Test substance :
04.15.2006

3.2.1 MONITORING. DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	: other: absorption/desorption
Media	: water - soil
Air	: % (Fugacity Model Level I)
Water	: % (Fugacity Model Level I)
Soil	: % (Fugacity Model Level I)
Biota	: % (Fugacity Model Level II/III)
Soil	: % (Fugacity Model Level II/III)
Method	: other: estimation using PCKOC (v 1.66)
Year	:
Remark	:

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	: Aerobic
Inoculum	:
Deg. product	:
Method	: Other:
Year	: 1974
GLP	:
Test substance	: Not known
Remark	: When tested in an enclosed aquatic system containing plankton, insects and snails, 2,6 DEA was considered readily biodegradable based on the organisms abilities to quickly eliminate it (Lu, PY, 1974).

04.15.2006

Type	: Aerobic
Inoculum	: other: mixed composite inoculum from pond water with or without 0.1% activated sewage sludge, nonadapted
Concentration	: 250 ug/mL

related to

Contact time	:	14 day(s)
Degradation	:	= .O% after 14 day(s) without sewage sludge; 3% with sewage sludge
Result	:	other: not readily biodegradable
Control substance	:	Aniline
Kinetic	:	7 day(s) = 100. % remaining, or 97% remaining with sewage sludge 14 day(s) = 100% remaining, or 97% remaining with sewage sludge
Deg. product	:	not measured
Method	:	
Year	:	1985
GLP	:	No
Test substance	:	As prescribed by 1.1-l .4

Remark : Aniline and other substituted anilines were examined for **persistance** in pond water, and pond water with sewage sludge innoculum. Aniline was extensively metabolized in pond water, with or without sewage sludge addition (10% remaining at 14 days without sewage sludge, 0% at 14 days with sewage sludge). 2,6 DEA, on the other hand, had 100% remaining without sludge, and 97% remaining with sewage sludge supplement. The authors found in other work that under conditions of simulated ensilage fermentation, 2,6 DEA had only 7% remaining, compared to 5% for aniline. (Lyons, CD et al, 1985, a,b)

04.15.2006

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

BCF	:	ca. 53.41
Elimination	:	
Method	:	other: estimate
Year	:	
GLP	:	
Test substance	:	
Remark		Estimated using BCF Program (v 2.15) from EPIWIN (v. 3.12)

Species	:	Gambusia (Fish, fresh water)
Exposure period	:	
Concentration	:	
BCF	:	120.
Elimination	:	no data
Method	:	
Year	:	1975
GLP	:	
Test substance	:	2,6 DEA

Remark : Lu, PY and Metcalf, RL, 1975

04.15.2006

3.6 ADDITIONAL REMARKS

Remark

04.15.2006

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	Static, Rainbow trout
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	ND.
LC50	:	= 24 mg/l .
Limit test	:	
Analytical monitoring	:	
Method	:	Other:
Year	:	1965
GLP	:	Yes
Test substance	:	as prescribed by 1 .1 - 1.4
Remark	:	McAllister, WA, 1965b
04.15.2006		

Type	:	Static, Bluegill Sunfish
Species	:	Lepomis macrochirus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	
LC50	:	= 30 mg/L .
Limit test	:	
Analytical monitoring	:	
Method	:	other:
Year	:	1965
GLP	:	Yes
Test substance	:	as prescribed by 1 .1 - 1.4
Remark	:	McAllister, WA, 1985a
04.15.2006		

Type	:	Static, Winter flounder
Species	:	Other: Pseudopleuronectes americanus
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	
LC50	:	= 29 mg/l (12.5-50 CL)
LC100	:	
Method	:	other:
Year	:	
GLP	:	Yes
Test substance	:	
Remark	:	EG&G Laboratories for Ethyl Corporation, 1963
04.15.2006		

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	Static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	46 hour(s)
Unit	:	mg/l
NOEC	:	

EC50 : = 21
Analytical monitoring :
Method :
Year : 1985
GLP : Yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Forbis, AD. 1985
04.15.2006

4 . 3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species :
Endpoint :
Exposure period :
Unit :
EC50 :
Method :
Year :
GLP :
Test substance :

Remark :
04.15.2006

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type :
Species :
Exposure period :
Unit :
EC50 :
Method :
Year :
GLP :
Test substance

Remark :
04.15.2006

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 **TOXICOKINETICS, METABOLISM AND DISTRIBUTION**

In Vitro/in vivo : In vivo
Type : Metabolic fate
Species : Rat
Number of animals
Males : 5 Long Evans per gavage group; 5 Sprague Dawley and 5 Long Evans in diet group
Females : 5 Long Evans in single gavage group
Doses
Males : 10 or 160 mg/kg gavage or 2707 ppm in diet
Females : 10 mg/kg gavage
Vehicle :
Route of administration : other: gavage or diet.
Exposure time : 1 day(s)
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product : No
Method : other:
Year : 1987
GLP : Yes
Test substance : other TS: Radiolabelled 2,6 DEA

Method : The following three dosing regimes were evaluated:
1. Single oral low-dose (10 mg/kg); m, f Long Evans rats
2. Single oral high-dose (160 mg/kg) m Long Evans
3. Single Diet dose for 24 hours; m Long Evans and Sprague Dawley

Result : After oral doses of 10 (single) or 160 (single) mg/kg or after a single dietary dose of 2707 ppm of ^{14}C-DEA, urine was the major route of elimination. Sprague-Dawley male rats excreted more in the urine (73.6%) than Long Evans (54.6%) when DEA was administered in the diet. When dosed by oral gavage, males eliminated 49.9-66.6% of the dose in the urine while females excreted 70.4%. a majority of the remaining dose for all groups was contained in the feces and cage wash. Only 0.36% was found in expired gases.
Only 0.031-0.066% of the DEA dose was found in the organs and tissues and 0.206-0.530% in the residual carcasses of the animals dosed with DEA. The nasal turbinates contained the highest relative levels of radioactivity for DEA. With the exception of the blood cell fraction there were no significant differences in the tissue distribution when DEA was administered in the diet or by oral gavage.
The whole body elimination kinetics for DEA was compatible with a two compartment model. For DEA, the alpha phase varied between 3.93 and 5.22 hours, while the beta phase was 50.4-216 hours.

Ridley, W P and J Warren, 1987.

04.15.2006

In Vitro/in vlvo : In vivo
Type : Distribution and localization
Species : Rats (Sprague Dawley) and Mice (CD-l)
Number of animals
Females : 2 rats, 2 mice

Doses
Females : 7 or 70 mg/kg C^{14} DEA
Vehicle : Corn Oil
Route of administration : Gavage
Exposure time : Single dose
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product : No
Method : other:
Year : 1993
GLP : Yes
Test substance : other TS: Radiolabelled 2,6 DEA

Method : The following dose regimes were evaluated:
1) Single oral dose (high)
2) Single oral dose (low)

Remark :
One female rat received a single oral dose of ^{14}C-DEA in corn oil, at 7 mg/kg (9.1 mg/kg actual) or 70 mg/kg (60.6 mg/kg actual). Similarly, one female mouse received a single oral dose of ^{14}C-DEA, at 7 mg/kg (6.5 mg/kg actual) or 70 mg/kg (70.6 mg/kg actual). 24 hours after dosing the animals were sacrificed. Tissue distribution and localization of ^{14}C-DEA was examined with whole body autoradiography. Autoradiographs were examined visually for the darkening produced by the presence of radioactive material. Assessment of relative levels was made by comparison of the darkened amount in the regions of the animals body. The films were also compared using densitometry.

Result : Whole body autoradiographs from female rats dosed at 7 or 70 mg/kg target doses showed localization of radioactivity in the intestine, stomach contents, preputial gland, liver, kidney, heart, lungs, peritoneal fat, skin, hair follicles and nasal mucosa. Very intense localization was seen in the lining of the tongue and esophagus. No significant differences were seen between the 7 and 70 mg/kg target dose levels.
The female mice, in contrast to the rats, did not show localization in the nasal mucosa, but had higher localization of radioactivity in the liver than did rats. Very intense localization was seen in the mouse gall bladder, lining of tongue and esophagus. Localization was also seen in the hearts, 'lungs and kidneys.

Hall, LJ and AGE Wilson, 1993

04.15.2006

5.1 .1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 1800 mg/kg bw (combined sexes)
Species : Rat
Strain : Sprague-Dawley
Sex : male/female
Number of animals : 94 (preliminary and definitive)
Vehicle : None
Doses : 500, 750, 1000, 1500, 2000, and 2500 mg/kg
Method : EPA proposed guidelines FR Vol 43 (163), 1978

Year	: 1980
GLP	: Yes
Test substance	: as prescribed by 1 .1 - 1.4
Remark	: All mortality occurred within a 3 day period post dosing, with an isolated delayed mortality on day 8 (1214 mg/kg). Clinical signs (decreased activity, decreased muscle tone, piloerection, dyspnea) were manifested at all dose levels, persisting for 6 days in most dose groups. LD 50 for males: 2500 (1910.2-3271.9) mg/kg; LD50 females 1450 (1047.2-2007.4) mg/kg, combined LD50: 1800 (1500.1 - 2159.9) mg/kg. Bier, CB and PH Oliviera, 1980.
Test condition	Vehicle: Material gavaged neat with volume adjusted for dose

04.15.2006

Type	: Oral LD50
Value	: g/kg
Species	: Rat
Strain	: CD
Sex	: Male
Number of animals	: 20
Vehicle	: None
Doses	: 1.35, 2.02, 3.04, 4.56 g/kg
Method	: other:
Year	: 1971
GLP	: no data
Test substance	: as prescribed by 1 .1 - 1.4
Remark	: Animals became cyanotic withn 24 hours of administration. Necropsy showed no significant pathological changes. All animals died at 4.56 g/kg; no animals died at 1.35 g/kg. Two of 5 animals died at the intervening doses. LD50 calculated by the method of Thompson-Weil was 2.69 g/kg with 95% confidence limits of 2.03 to 3.56 g/kg. Tulane University, for Ethyl Corporation, 1971

04.15.2006

5.1.2 ACUTE INHALATION TOXICITY

Type	: Inhalation
Value	mg/m^3
Species	: Rat
Strain	:
Sex	: Male
Number of animals	: 50
Vehicle	:
Doses	: 0, 210, 220, or 4700 mg/m^3
Exposure time	: 1, 4 or 6 hours
Method	:
Year	: 1974
GLP	: No
Test substance	As prescribed in 1.1-1.4
Remark	: Rats were exposed in a rectangular chamber 280 liters in volume. Vapor was generated by passing air through the compound contained in two bubbling towers joined in series. A thermal blanket wa applied to the bottom of each tower to maintain the temperature of the liquid above room temperature. Air supplied to the chamber ranged in temperature from 25.5 to 9°C. Chamber temperatures averaged 30.7°C. Mist was generated in a

one liter flask using an aspirator. Air flow through the generator was 35 liters per minute. Air samples were analyzed for test article. Blood samples were taken from the rats the day preceding exposure, and at 18 hours following a single exposure. Hemoglobin, hematocrit and methemoglobin were measured.
Rats exposed to 210 mg/m^3 survived single one and four hour exposures, and sixteen exposures for six hours. Rats exposed to 4700 mg/m^3 for a single six hour period died within 3 days. Animals given sublethal exposures salivated during exposure and were lethargic, and showed purplish color to ears, paws and scrotum. Coloring returned to normal within a few hours postexposure. Animals given lethal exposure showed labored respiration and coma postexposure. Methemoglobin levels 18 hours post exposure slightly increased from preexposure values (up to 3%). Microscopic examination of the lungs of rats exposed for 1 hour to 210 mg/m^3 showed accumulation of macrophages in the alveolar spaces and mild infiltration by leucocytes within alveolar septa. After 4 hour exposure, acute focal pneumonia was present extending over 15% of the pulmonary tissue in 5 of 6 rats. One animal had focal pulmonary hemorrhages. Animals exposed 14 times for 6 hours per exposure and sacrificed two weeks after the exposure had confluent bronchial pneumonia. Livers in these animals were markedly congested, and showed slight to moderate parenchymal degeneration of hepatocytes. Three of those animals had cloudy swelling in the kidneys. Animals exposed to the highest concentration died within three days of exposure and had extensive hemorrhage and edema of the lungs. Focal necrosis was seen in the livers, and cloudy swelling in the kidneys.
Witherup, S, for Ethyl Corporation, 1974

: .

04.15.2006

5.1.3 ACUTE DERMAL TOXICITY

Type	:	Dermal LD50
Value	:	1.085 g/kg bw
Species	:	Rabbit
Strain	:	New Zealand White
Sex	:	male/female
Number of animals	:	41
Vehicle	:	Neat
Doses	:	262 to 6545mg/kg in main study
Method	:	Other: Federal Hazardous Substances Labelling Act (1965)
Year	:	1974
GLP	:	No
Test substance	:	as prescribed by 1 .1 - 1.4

Remark : Four rabbits per dose group (two with intact skin sites and two with abraded sites) were used per dose groups ranging from 0.28 ml/kg (262 mg/kg) to 7.0 ml/kg (6545 mg/kg). Material stayed in contact with skin for 24 hours. No deaths occurred at 262 or 393 mg/kg, and all animals died at 2992 mg/kg to 6545 mg/kg, at less than 24 hours and up to 7 days. One animal each was tested at dose levels of 10, 16, 24, and 36 ml/kg, and all dosed at those levels died in less than 24 hours to 3 days. Clinical observations included weakness, decrease in respiration, reduction in body temperature, coma and gradual respiratory failure. All rabbits lost weight following exposure, but survivors recovered losses by end of second week. Using the moving average method, LD50 was estimated to be 1 .16 +/- 0.43 ml/kg (1085 +/- 402 mg/kg).
Histopathology of the intact skin sites showed erythema, edema, and

moderate lymphocytic infiltration. Abraded skin sites showed superficial ulcers extending to middermis.

Note: previous work at this laboratory in rats had shown that 2,6 DEA applied to intact skin of rats for 6 hours had caused death in all animals when dose was 9.5 g/kg; rats survived when dose was less.

Witherup, S., for Ethyl Corporation, 1974

04.15.2006

Remark :
04.15.2006

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	Rabbit
Concentration	:	0.7 g
Exposure	:	Semiocclusive
Exposure time	:	24 hours
Number of animals	:	6
Vehicle	:	
PDII	:	2.7 (used intact and abraded site scores)
Result	:	
Classification	:	Not classified as irritant
Method	:	Federal Hazardous Substances Labelling Act
Year	:	1974
GLP	:	No
Test substance	:	as prescribed by 1 .1 • 1.4

Remark : 2,6 DEA was applied to intact and abraded sites for 24 hour contact. Scoring for erythema and eschar and edema were made at 24 and 72 hours. Primary irritation score was calculated from intact and abraded skin sites, at both time points. Classification as an irritant, by the criteria at the time of the test, required a score of 5 or more. Since the Primary Irritation Score calculated in this test was 2.7, the material was not considered an irritant. However, just considering intact skin sites, three animals had positive scores for erythema at 24 hours; one at 72 hours. Three had positive scores for edema at 24 hours, and one continued to have a positive score at 72 hours. This would indicate some potential for irritation.
Witherup, S, for Ethyl Corporation, 1974

04.15.2006

5.2.2 EYE IRRITATION

Type		Eye Irritation
Species	:	Rabbit
Number of animals	:	7
Vehicle	:	
Result	:	
Classification	:	Irritant
Method	:	Federal Hazardous Substances Labelling Act

Year : 1974
GLP : No
Test substance : As prescribed by 1 .1-1 .4

Remark : After 24 hours, 3 of 7 rabbits showed severe reactions consisting of sweling and erythema in the tissues around the eye, severe palpebral edema with partial eversion or closing of the eyes, cloudiness of the cornea and purulent discharge. Three animals showed mild reaction such as mild erythema of the external surface and mild to moderate palpebral conjunctivitis with no involvement of the cornea. One animal had no remarkable change. There was no iris involvement. There was little change in scoring at 48 and 72 hours. All animals had recovered by the 10th day. Since 5 of 7 animals showed positive scores for erythema and edema (criteria for classification is 4 or more), 2,6 DEA was considered an eye irritant. Microscopic examination of the eyes showed marked edema with infiltration by lymphocytes and polymorphnuclear leucocytes within the eyelids. Conjunctiva was markedly hyperemic. Minute ulcerations were present in the cornea.
Witherup, S, for Ethyl Corporation, 1974.

04.152006

5.3 SENSITIZATION

Type : Guinea Pig Contact Dermal Irritation/Sensitization
Species : guinea pig
Concentration : 1st: Induction: 0.05 ml first injection, 0.1 ml nine others, intracutaneous
2nd: Challenge: 0.05 ml intracutaneous

Number of animals : 10: 6 for test, 4 for positive control
Vehicle :
Result : not sensitizing, not primary skin irritant, not fatiguing agent
Classification : not sensitizing
Method : Other
Year : 1979
GLP : No
lest substance : As prescribed in 1.1 to 1.4

Remark : A group of 10 guinea pigs were used in the study. Backs were clipped of hair. Six guinea pigs were induced with intracutaneous injections of test article using a 26 gauge needle. Injections were given every other day until a total of 10 injections were given. The first injection used a volume of 0.05 ml, the other nine used a volume of 0.1 ml. Two weeks after the tenth injection, a challenge injection was made using the 0.05 ml volume. Skin scores were made at 24 and 48 hours after challenge injection. Four guinea pigs were treated similarly using 0.1% dinitrochlorobenzene solution in ethylene dichloride as a positive control. None of the animals given DEA reacted to sensitizing or challenge injections. Three of the four positive control animals reacted more strongly at challenge than on the tenth induction day.

Gabriel, KL, for Ethyl Corporation, 1979

08.02.2002

5.4 REPEATED DOSE TOXICITY

Type : Repeated dose, dermal, 28 day
Species : Rat

Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Dermal
Exposure period	:	28 days
Frequency of treatm.	:	Once a day for 6 hours, five days per week
Post exposure period	:	
Doses	:	0, 100, 300 or 1000 mg/kg bw
Control group	:	One control group with saline
NOAEL	:	= 100 mg/kg bw
Method	:	OECD Guideline 410 "Repeated Dose Dermal Toxicity: 21/28-day Study"
Year	:	1985
GLP	:	Yes
Test substance	:	as prescribed by 1 .1 - 1.4

Remark : 2,6 DEA: NOAEL (dermal, rat) = 100 mg/kg bw
Test article was applied neat to shaved back skin on rats (1 O/sex/group) with a collar used to prevent ingestion. After six hours, the material was wiped clean and the collar removed. Concurrent control animals had saline applied in the same manner. 30 tissue types were examined histologically from high and control animals; skin, kidneys and spleens were also examined from low and mid dose animals. Three high dose animals died on days 9-10. Moderately decreased body weight gains were seen in high dose males, and a lesser decrease in gains were seen in mid dose males and high dose females.
Increased reticulocytes were seen in high dose male and female blood samples. Very slight > SGPT and/or SGOT levels were noted in mid and high dose animals, associated with slight increases in liver weights.
Treatment related skin lesions (superficial inflammation) and very slight histopathological lesions of the spleen (females, increased hemosiderin) and kidneys (males, increased eosinophilic hyaline droplet formation in cytoplasm of cortical renal tubular epithelial cells) were seen after exposure for one month to 100 mg/kg test article. Decreased weight gain and slightly increased liver weights and serum enzymes were noted at the mid and high dose. The systemic effects at the high dose were very minimal and probably not biologically significant.

Reyna, MS, for Monsanto Company, 1985

Test substance :
14.02.2002

Type	:	Repeated dose, inhalation, 30 day
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Inhalation
Exposure period	:	30 days
Frequency of treatm.	:	Once a day for 6 hours, five days per week for total of 22 exposures
Post exposure period	:	
Doses	:	
Control group	:	One control group, no treatment
NOAEL	:	
Method	:	
Year	:	1976
GLP	:	No
Test substance	:	as prescribed by 1 .1 - 1.4

Remark : 2,6 DEA: NOAEL (inhalation, rat) = 0.073 mg/L average analytical vapor concentration
One group of rats (5 male, 5 female) were exposed to an average analytical vapor concentration of DEA of 0.073 mg/L. Test article was heated to a temperature of 36'C to generate the vapor. A concurrent control animals had no treatment of any kind. At the end of the 30 day

period, animals were sacrificed and examined for gross pathology. No animals died during the test period, and no abnormal behavior was noted. Average body weight gains for treated animals were below the average gains by control animals, but were within historical values. No gross pathological differences were noted.

Industrial Bio-Test Laboratories for Monsanto Company, 1976.

Type	:	Inhalation
Value	:	mg/L
Species	:	Dogs
Strain	:	Beagle
Sex	:	Male
Number of animals	:	4 (2 control, 2 exposed)
Vehicle	:	
Dose	:	0.27 mg/L (measured)
Exposure time	:	6 hours; 5 days per week for 4 weeks.
Method	:	
Year	:	1974
GLP	:	No
Test substance	:	As prescribed in 1 .1-1 .4

Remark : Dogs were exposed in a hexagonal chamber 900 liters in volume. Vapor was generated by passing air through the compound contained in two bubbling towers joined in series. A thermal blanket wa applied to the bottom of each tower to maintain the temperature of the liquid above room temperature. Air supplied to the chamber ranged in temperature from 25.5 to 9'C. Chamber temperatures averaged 30.7'C. Mist was generated in a one liter flask using an aspirator. Air flow through the generator was 35 liters per minute. Air samples were analyzed for test article. Blood samples were taken from the dogs on two days preceding exposure, 30-45 minutes following an exposure, and 48 hours after final exposure. Hemoglobin, hematocrit, methemoglobin and clinical chemistries were measured.

Dogs exposed to 2,6 DEA survived twenty 6 hour exposures, but one of the two exposed dogs died after the 20th exposure. The surviving exposed dog had elevated alkaline phosphatase activity and a sharp decrease in cholesterol levels in clinical chemistry determinations. The surviving exposed dog was sacrificed two days after exposures, and had pale liver grossly, which histologicallyshowed diffuse acute liver necrosis. Kidneys had degeneration of epitheliumof the convoluted tubules. Macrophages were present in alveolar spaces of the lungs. The animal that died after 20 exposures had marked icterus. The liver had marked diffuse liver necrosis. The kidney showed degeneration of convoluted tubules, and the spleen and intestinal walls were hyperemic.

Witherup,S, for Ethyl Corporation, 1974

Test condition : .

04.15.2006

Type	:	Repeated dose, oral, 20 days
Species	:	Rat
Sex	:	Male
Strain	:	Fischer 344
Route of admin.	:	Oral
Exposure period	:	5, 10 or 20 days
Frequency of treatm.	:	
Post exposure period	:	None
Doses	:	
Control group		
NOAEL	:	
Method	:	

Year	:	1963
GLP	:	Not known
Test substance	:	As prescribed in 1 .1-1 .4
Remark	:	The toxicity of ring substituted dialkylanilines, aniline, o-toluidine, 2,4 dimethylaniline, 2,6 diethylaniline, 2,6 methyl ethylaniline, 2,6 diisopropyl aniline, and methylene bis 2,6 diisopropyl aniline were studied in rats. Doses varied between 67.5 to 50.4 mg/kg for 5, 10, or 20 days. Tissues examined were liver, spleen, thyroid, urinary bladder and kidneys. Hemosiderosis occurred in spleens of rats in all groups. Liver sections showed periacinar vacuolar changes in all groups; biliary hyperplasia, swelling and periacinar necrosis were other effects observed. There were no microscopic lesions in kidney, spleen, thyroid or urinary bladder. Short, CR, et al., 1983
Type	:	Repeated dose, dietary, 28 days
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	Dietary
Exposure period	:	28 days
Frequency of treatm.	:	7 day/week
Post exposure period	:	None
Doses	:	0, 0.07%, 0.15%, 0.3% in diet (approx. 0, 70, 150, and 300 mg/kg)
Control group	:	Yes, untreated feed
NOAEL	:	
Method	:	
Year	:	1981
GLP	:	Yes
Test substance	:	As prescribed in 1 .1-1 .4
Remark		10 male and 10 female rats per group were fed diet containing DEA at 0.07%, 0.15%, 0.3% of the diet. There was a slight decrease in body weight gain and food consumption at all levels. No other indications of toxicity were noted. Hematologic evaluation, including platelet count, methemoglobin concentration and the presence of Heinz bodies, and blood chemistries were performed at termination. Organ weights were measured, and histopathology was performed on brain, liver, kidneys, spleen, adrenals, heart, thyroid, parathyroid, and sternebrae (bone marrow) from all rats in control, mid and high dose groups. There were no deaths, but a low dose animal was sacrificed in poor condition by day 9. Larson, WJ and RW Naismith, for Ethyl Corporation, 1981

04.15.2006

Type	:	Repeated dose, inhalation, 90 day
Species	:	Rat
Sex	:	male/female
Strain	:	Charles River COBS
Number:		15 male, 15 female per group
Route of admin.	:	Inhalation
Exposure period	:	68 exposures in 90 days
Frequency of treatm.	:	6 hours daily, 5 days/week
Post exposure period	:	None
Doses	:	0, 10 or 100 mg/m3 (acutal, 0, 10 +/- 2.5; 90 +/- 16.4 mg/m^3)
Control group	:	yes, concurrent no treatment
NOAEL		=
LOAEL		> 100 mg/m^3 mg/kg bw
Method		
Year	:	1979
GLP	:	
Test substance	:	As prescribed in 1 .1-1 .4

Remark	:	Exposures were conducted in stainless steel and glass inhalation chambers with 500 liter capacity. Vapor was generated by passing a stream of clean, dry air over undiluted test materail headted during exposure (38°C for low dose group; 55°C for high dose group. The air/vapor mixture was passed through 1000 ml Erlenmeyer flasks to trap condensed test vapor before entering exposure chambers. Average nominal vapor concentratoins were calculated daily by dividing the difference between generator weight loss and trap weight gain by total volume of air used in the test. Analytical concentrations were also determined with a gas chromatography method. There were no deaths or clinical observation differences in the animals. Weight gains in male treated animals were higher than control; females were the same. Blood analysis, and chemistries (blood glucose, BUN, SAP, SGPT, and methemoglobin) were comparable at each interval, as were urinalysis values. No gross or histopathological alterations were attributed to the test article. There were some differences in some organ weights, but no consistent or dose related effects. Industrial Bio-Test Laboratories, for Monsanto Company, 1979

04.152006

Type	:	Repeated dose, dietary, 90 days
Species	:	Rat
Sex	:	male/female
Strain	:	Sprague Dawley
Number		270 animals(5 m, 5 f prestudy; 25 m, 25 F in control and groups 2-4, 10 m, 10 f in group 5; additional 10 m, 10 f in control and group 4 for 45 day sacrifice)
Route of admin.	:	oral feed
Exposure period	:	90 days
Frequency of treatm.	:	Daily
Post exposure period	:	None
Doses	:	Groups I-5: (0, 0.03%, 0.12%, 0.48% of diet; 0.72% for pathological exam only)
Control group	:	Yes
NOAEL	:	=
NOEL	:	=
Method	:	
Year	:	1982
GLP	:	Yes
Test substance	:	As prescribed in 1 .1-1 .4

Remark	:	At the 45 day sacrifice of 10 males and 10 females from the control and 0.48%, the treated animals had slightly heavier livers and slightly elevated blood cholesterol levels. No pathology was noted in organs from sacrificed animals, either microscopically or macroscopically. No deaths had occurred in any of the 5 groups, nor were clinical signs altered. Retarded rate of body weight gain and reduced food consumption was noted in females at this point in the study. At the 90 day end of the study, treatment related effects involved food consumption, body weight gain, one serum component, and liver weight. Female food consumption and rate of body weight gain were mildly to moderately reduced related to dose, but not in males. This was thought related to palatability. Serum cholesterol levels in males and females were mildly elevated at low, and mid dose, and moderately at 0.48%. Liver weights were reduced in treated animals compared to controls, significantly so at 0.72%. No other notable effects were seen in hematology, blood chemistry, urinary components, clinical signs or histopathology. Larson, WJ and RW Naismith, for Ethyl Corporation, 1982

04.15.2006

5.5 GENETIC TOXICITY 'IN VITRO

Type	: Ames test
System of testing	: Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA1 00
Test concentration	: +/- S9: 0.01, 0.05, 0.10, 0.50, 1 .O ul/plate; from 1% v/v solution in DMSO
Cycotoxic concentr.	: > 1 .O ul/plate of a 1% solution
Metabolic activation	: with and without S-9 from Aroclor 1254 induced male Sprague Dawley rats
Result	: Negative
Method	: other: based on Ames et. al. (1975)
Year	: 1977
GLP	: no data
Test substance	: as prescribed by 1 .1 - 1.4
Remark	: Schechtman, LM, for Ethyl Corporation, sponsor, 1977
Test condition	: Quality Assurance was similar to GLP

04.15.2006

Type	: In vitro point mutation
System of testing	: Chinese hamster ovary (CHO) cells/ HGPRT locus
Test concentration	: +/- S9: 300-500 ug/ml in absence, 200-400 ug/ml in presence
Cycotoxic concentr.	: At highest doses tested
Metabolic activation	: with and without, Aroclor induced S-9
Result	: Negative
Method	:
Year	: 1987
GLP	: Yes
Test substance	: As described in 1.1-l .4
Remark	: Slightly eleveated mutation frequencies were seen at several concentrations producing significant cytotoxicity, but these increases were weak, and not statistically significant. Additional concentrations were tested to clarify inconsistent results. Six concentrations of DEA ranging from 450 to 475 ug/ml and 275-400 ug/ml respectively were used in each experiment. Only weak and sporadic increases in mutation frequency were noted following incubatoin of Chinese hamster ovary cells with 2,6 diethylaniline. These increases were neither statistically significant nor dose related. Therefore, 2,6 DEA is not considered to be mutagenic at the hypoxanthine-guanine phosphoribosyl transferase (HGPRT) locus of Chinese hamster ovary cells. Flowers, LJ, Monsanto Company, 1987
	:.

Type	: Cell transformation
System of testing	: BALB/3T3 Clone A31 mouse embryo cells
Test concentration	: 0.5 and 0.1 ul/ml
Cycotoxic concentr. :	
Metabolic activation	: Hepatic tissue homogenate from F344 male rats induced with Aroclor 1254
Controls	DMSO for solvent control, MNNG without activation, Benzo(a)pyrene with activation
Result	: Negative
Method	: other: Schechtman and Kouri, 1977
Year	: 1980
GLP	: Quality Assurance procedures like GLP
Test substance	: As prescribed by 1.1-1.4
Remark	: Without activation: Relative to control, colony forming efficiency of 3T3 cells exposed to test article were 45-89%. Positive control (MNNG) reduced colony forming efficiency to 53%. Of the doses employed, in the

absence of exogenous metabolic activation, test article failed to induce both Type II and Type III morphologically transformed foci.
With activation: Positive control was Benzo(a)pyrene. Relative to control, colony forming efficiency of 3T3 cells exposed to test article were 42-87%. Positive control reduced colony forming efficiency to 42%. Of the doses employed, in the presence of exogenous metabolic activation, test article failed to induce both Type II and Type III morphologically transformed foci.
Schechtman, LM, for Ethyl Corporation, 1980 a and b

14.02.2002

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA100
Test concentration	:	0.003 to 3.00 ul/plate with activation, 0.0015 to 2.25 ul/plate in absence of activation
Cycotoxic concentr.	:	> plate
Metabolic activation	:	with and without, male rat Aroclor induced S-9
Result	:	
Method	:	
Year	:	1983
GLP	:	
Test substance	:	As described 1.1-l .4

Remark : Very slight but apparently dose-related increases in revertants were observed in glass and plastic petri dishes with activation. In absence of activation, slight increase in revertants seen in plastic but not glass dishes. Responses were never more than twice those in solvent controls, and not always reproducible. Conclusion was that 2,6 diethylaniline was weakly mutagenic in TA 100 in the presence of activation, but the low level of reponse was not considered to be biologically significant.
Flowers, LJ, for Monsanto Company, 1983,

04.15.2006

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98 and TA100
Test concentration	:	0.25 to 3,000 ug/plate
Cycotoxic concentr.	:	> 1 mg/plate without activation in TA1 00 and 3 mg and above with plate
Metabolic activation	:	with and without, male rat Aroclor 1254 induced S-9
Result	:	Negative in TA98 with and without activation and TA 100 without activation; weakly mutagenic in TA 100 in presence of activation
Method	:	Ames, 1975
Year	:	1986
GLP	:	
Test substance	:	As described 1 .1-1 .4

Remark : In absence of activation, slight increase in revertants seen with TA 100. Responses were never more than twice those in solvent controls. Mutagenic potency was low: 0.007-0.009 revertants/nmole
Kirk, AM, for Monsanto Company, 1986

04.15.2006

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98, TA1 00, TA 1535, TA 1537
Test concentration		0, 0.05, 0.15, 1.50, 5.0 mg/plate
Cycotoxic concentr.	:	5mg/plate
Metabolic activation	:	with and without, various sources of S-9
Result		Negative in TA98 and TA 1537with and without activation from any source Marginal equivocal results for TA 100 and TA 1535
Method	:	Ames, 1975
Year		1990
GLP	:	Yes
Test substance	:	As described 1 .1-1 .4

Remark : Control substances used in the TA98 and TA 100 tests were 4-nitroquinoline-N-oxide (without S-9) and 2-aminoanthracene (with S-9). 2-aminoanthracene was used as the positive control for TA1535 and TA1537 (with S-9). Sodium nitrite was used with TA 1535 (without S-9) and 9-aminoacridine was used with TA 1537 (wihout S-9). DMSO was the solvent used as vehicle control. Frozen nasal turbinate S-9 preparations were used from male Long Evans rats, male CD-l mice, and male and female squirrel monkeys. None of the species were treated with enzyme inducers prior to S-9 isolation. The procedures for the Ames test used plate incorporation.

For TA 100 and TA 1535, observed increases in revertants/plate were limited to 1.5 to 2 fold over control values, generally at 1.5 mg/plate. Although there were some activity in the absence of S-9, more consistent activity was observed in the presence of nasal turbinate S-9. There were no substantial differences between rat, mouse or monkey S-9, but the responses were marginal, limiting the comparison.
Kier, LD and Stegeman, SD, for Monsanto Company, 1990

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus Test
Species	:	Mouse
Sex	:	Male and female
Strain	:	BS-1
Number		Four female, four male mice per group
Route of admin.	:	Intraperitoneal (i.p.)
Exposure period	:	Split dose separated by 24 hours
Doses	:	100 or 200 mg/kg
Result	:	Negative
Method	:	Schmid, W. 1975
Year	:	1980
GLP	:	Quality Assurance procedures like GLP
Test substance	:	As prescribed in 1.1-l .4

Remark : 2,6 DEA was suspended in 0.25% methylcellulose. Two drops of a 5% solution of Tween 80 were added, and solutions vortexed to assure suspension. In a preliminary range find study, mice at 100 mg/kg showed increased spontaneous activity, and brief ataxia after fist dose and immediately following second dose. At 300 mg/kg, all mice had ataxia, 2 of 6 had mild convulsions, and one lost righting reflex after first dose. After second dose, all mice had severe ataxia and convulsions, and three of six mice had loss of righting. Doses used in the micronucleus study were 100 and 200 mg/kg. Positive control was triethyleneamine at 0.5 mg/kg, and as negative control, 0.25% methylcellulose at 20 ml/kg. All mice were sacrificed with CO2 asphyxiation six hours after the second dose. Femurs were removed, and bone marrow aspirated into fetal calf serum. Suspensions were centrifuged, and slides were prepared from the sediment. After slide staining and clearing processes, one thousand polychromatic erythrocytes were examined for micronuclei under the microscope. Frequency of micronucleated cells was expressed as % micronucleated cels versus total polychromatic erythrocytes. Mean values for micronuclei/1000 polychromatic erythrocytes were 25.25 (negative control), 69.5 (positive control), 29.63 (DEA, 200 mgikg), and 38.88 (DEA, 100 mg/kg). Note: slides from this study were reevaluated in 1982 to reflect more current methodologies for determining micronuclei. Values

from that reevaluation were 2.29 (negative control), 17.67 (positive control), 2.75 (DEA 100 mg/kg) and 3.50 (DEA 200 mg/kg).
Naismith, RW and RJ Matthews, for Ethyl Corporation, 1980

04.15.2006

5.7 CARCINOGENICITY

Species	: Rat
Sex	: male/female
Strain	: Sprague-Dawley
Number	Control (100 m, 100 f), treatment groups (80 m, 80 f)
Route of admin.	: Dietary
Exposure period	: 104 weeks
Frequency of treatm.	: Daily
Post exposure period	: None
Doses	: 0, 0.02%, 0.16%, or 0.32% of the diet
Result	: Negative
Control group	: yes, concurrent, no treatment
Method	:
Year	: 1986
GLP	: Yes
Test substance	: As prescribed in 1.1-l .4

Remark : 2,6 DEA was incorporated into standard laboratory feed and fed ad libitum to 4 groups of Sprague Dawley rats for a period of no less than 731 days. Clinical biochemical analysis and hematological evaluations including methemoglobin analysis was conducted on a preclinical test group, and from 10 rats per sex/group at 6, 12, 18 months and at termination. Urine analysis was conducted pretest and at 6 month intervals.
Gross lesions, and a standard set of tissues were saved for microbiological analysis. Male reproductive organs included testes, prostate, epididymides, and seminal vesicles. Female reproductive organs sampled were Fallopian tubes, ovaries, uterus, cervix, mammary gland, and vagina. Test article in the diet did not alter survival, food consumption, clinical pathology values, organ weight data or incidence of neoplastic or non-neoplastic lesions in the rats. A body weight gain retardation was observed in high dose male (7%) and female (25%) rats at each six month interval over the course of the test. Survival (control versus high dose) was 74.3% vs 78% in males and for females 41.4% vs 36%.
Naismith, RW and RJ Matthews, for Ethyl Corporation, 1986.

04.15.2006

5.8.1 TOXICITY TO FERTILITY

Remark
04.15.2006

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Type:

Species	: Rat
Sex	: Female
Strain	: Sprague-Dawley
Route of admin.	: Gavage
Exposure period	: on gestational days 6 through 15
Frequency of treatm.	: Daily
Duration of test	: 21 days
Doses	: 0, 50, 250, and 500 mg/kg/day

Control group	:	yes, concurrent vehicle
other: NOEL Maternal Tox.	:	None
other: NOEL Teratogenicity	:	>= 500 mg/kg bw
Result	:	Not embryotoxic or teratogenic to 500 mg/kg, but fetotoxic (decreased fetal weight and retarded stemebrae ossification) at 500 mg/kg in presence of maternal toxicity
Method	:	
Year	:	1986
GLP	:	Yes
Test substance	:	As prescribed in 1.1-l .4
Remark	:	2,6 DEA mixed with corn oil was administed by gavage to 4 groups of mated rats (24 for control, low and mid dose) and 29 for high dose group during days 6-l 5 of pregnancy. All dams were sacrificed on day 20, and gross postmortem exams conducted. Fetuses were examined for extermal malformations and half were examined by microdissection. The other half were stained and examined for skeletal defects. No mortality occurred in control, low or mid dose dams. Five high dose females died or were sacrificed moribund during the study. Physical signs of toxicity were seen in all groups and included salivation, anogenital staining, and decreased maternal body weight gains. Pregnancy rates (95.8%, 1 OO.O%, 95.8%, 96.6%) and uterine implantations were comparable, although there was a slight increase in resporptions in the high dose groups, primarily due to a single female with 10 resorptions and 2 viable pups. Mean fetal body weights were comparable in control, low and mid dose pups, but there was about a 9% lower average weight in the high dose group. No external, visceral, or skeletal malformations were noted that could be treatment related. However, there was an increased incidence of unossified stemebrae in high dose pups, consistent with retarded fetal development. Schroeder, RE, for Monsanto Company, 1986

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5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.8 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

IUCLID

Data Set

Existing Chemical	:	ID:
Memo	:	
CAS No.	:	578-54-I
EC No.	:	**209-424-2**
EINECS Name	:	Ortho-ethylaniline
CAS Name	:	Benzeneamine, **2-ethyl**
Common name	:	OEA
Molecular Formula	:	$C_8H_{11}N$

Producer related part		
Company	:	Albemarle Corporation
Creation date	:	

Substance related part		
Company	:	Albemarle Corporation
Creation date	:	

Status	:	
Memo	:	

Printing date	:	
Revision date	:	
Date of last update	:	

Number of pages	:	

Chapter (profile)	:	Chapter: **1, 2, 3, 4, 5, 6, 7, 8,** 10
Reliability (profile)	:	Reliability: without reliability, **1, 2,** 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety **Dataset,** Risk Assessment, Directive **67/548/EEC, SIDS**

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	other: sole-representative notifier
Name	:	
Contact person	:	
Date	:	
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	Manufacturer
Name of plant	:	Albemarle
Street	:	
Town	:	
Country	:	
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

04.15.2006

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

Remark : The read across of data from compounds of similar chemical structure for the purpose of safety evaluation is not **a** new concept. Data on several identical endpoints are provided in the dossiers for different ring substituted anilines (aniline, **2,6** DEA, 2 methyl 6 ethyl aniline, ortho ethyl aniline) The data show the similarity of toxicological and ecotoxicological properties of these substances. Therefore, it is considered scientifically acceptable to read across data on short-term toxicity and ecotoxicity studies and local effects to other aniline substances without particular tests available. For tests involving the use of experimental animals the read across of data is further supported by animal welfare reasons.

The category approach has already been used for N-substituted anilines by the American Chemical Council Mono Aromatic **Amines** and Nitroaromatics panel.

04.15.2006

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name
Smiles Code : cl cccc(N)c1 (CC)
Molecular formula : C8 H11 N
Molecular weight : 121.18 (Lide, DR, ed, 1999)
Petrol class

1 GENERAL SUBSTANCE INFORMATION

Purity type : Typical for marketed substance
Substance type : Organic
Physical status : Liquid
Purity : = . > 98 % w/w
Colour
Odour

28.02.2002

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

Remark : CAS name
Remark Benzeneamine, 2-ethyl

Remark : EINECS
Remark 2-Ethylaniline

Remark Aniline, 2 ethyl
Remark 2 ethylbenzeneamine

Remark : Aniline, 2-ethyl
Remark 2 ethylphenylamine

Remark 2-ethylbenzamine
Remark o-ethylaniline

Remark : Trade name
Remark OEA

Remark : Trade name
Remark ethylaniline, 2 (OEA)

Remark : Trade name
Remark 2 OEA

Remark : Trade name
Remark Ortho ethylaniline

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No : 579-66-8
EC-No : 209-445-7
EINECS-Name : 2,6-Diethylaniline
Molecular formula : $C_8H_{15}N$
Value : <= 0.8 % w/w

Purity : typical for marketed substance
CAS-No : 62-53-3
EC-No : 200-539-3
EINECS-Name : Aniline
Molecular formula : C_6H_7N
Value : <= 0.1 % w/w

28.02.2002

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling : None required
Specific limits : No
Symbols :
Nota :
R-Phrases :
S-Phrases :

Remark :
04.15.2006

1.6.2 CLASSIFICATION

Classified : None required
Class of danger :
R-Phrases :
Specific limits :
1st Concentration :

2nd Concentration :
3rd Concentration :
4th Concentration :
5th Concentration :
6th Concentration :
7th Concentration :
6th Concentration :
1st Classification :
2nd Classification :
3rd Classification :
4th Classification :
5th Classification :
6th Classification :
7th Classification :
6th Classification :

04.15.2006

1.6.3 PACKAGING

1.7 USE PAT-TERN

OEA is used as an intermediate in synthesis of dyestuffs, pharmaceuticals, pesticides and other products. (Lewis, R.J., ed,. 1997)

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

OEA is prepared by orthoalkyiation chemistry. This involves the reaction of aniline with ethylene catalyzed by aluminum anilide catalyst. The catalyst is prepared by the reaction of aniline with triethytaluminum.

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

Type	:
CAS-No	:
EC-No	:
EINECS-Name	:
IUCLID Chapter	:

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Type	Melting Point
Value	**: = -44 / -46.5%**
Sublimation	
Method	
Year	
GLP	
Test substance	: as prescribed by 1 .1 – 1.4
Remark	: Albemarle MSDS / Literature value **(Daubert,** TE, 1989)
04.15.2006	

Type	Melting Point
Value	**: = 2288°C**
Sublimation	
Method	:
Year	
GLP	
Test substance	: as prescribed by 1 .1 – 1.4
Remark	: Estimated by MPBPWIN **(v1.41)** in EPIWIN **(v3.12)**
04.15.2006	

2.2 BOILING POINT

Type	: Boiling Point
Value	: = 214% at 760 **mmHg** / 209.7%
Method	
Year	
GLP	
Test substance	: as prescribed by 1.1 - 1.4
Remark	: Albemarle MSDS / Literature value **(Daubert,** TE, 1989)
04.15.2006	

Type	: Boiling point
Value	**: = 223.43%**
Method	
Year	
GLP	
Test substance	: as prescribed by 1.1 - 1.4
Remark	: Estimated by MPBPWIN **(v1.41)** in EPIWIN **(v3.12)**
04.15.2006	

2.3 DENSITY

Type	: Density
Value	: **= . 0.98 @ 20°C**
Method	
Year	:
GLP	

Test substance : as prescribed by 1.1 - 1.4

Remark : Literature Value (Lewis, RJ, 1997)
04.15.2006

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Type : Vapor pressure
Value : = 0.11 mm Hg at 20°C / 0.170 mmHg at 25°C
Method
Year
GLP
Test substance : as prescribed by 1 .1 - 1.4

Remark : Albemarle MSDS / Literature value (Daubert, TE, 1969)
04.15.2006

Type : Vapor pressure
Value : = 0.222 mmHg at 25°C
Method : Mean of Antoine and Grain methods
Year
GLP
Test substance : As prescribed by 1 .1 - 1.4

Remark : Estimated from EPIWin (v. 3.12)
04.15.2006

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : 1.74 .
pH value . .
Method
Year : 1995
GLP : No data
Test substance : As prescribed by 1.1 - 1.4

Remark : Literature Value (Hansch, C. And Leo, A., 1995)
04.15.2006

Partition coefficient : octanol-water
Log pow : 2.11.
pH value . .
Method
Year : 2006
GLP
Test substance : as prescribed by 1 .1 - 1.4

Remark : Estimated by Log Kow (version 1.67) from EPIWIN (v. 3.12)
04.15.2006

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	: Water
Value	: = 0.4% weight at 20 °C
pH value	: .
concentration	: at °C
Temperature effects	
Examine different pot.	
pKa	: at 25 °C
Description	
Stable	
Deg. product	
Method	: other:
Year	:
GLP	:
Test substance	: as prescribed by 1 .1 - 1.4
Remark	: Albemarle MSDS
04.152006	

Solubility in	: Water
Value	: = 2117.9 mg/L
pH value	
concentration	: at 25 °C
Temperature effects	
Examine different pol.	
pKa	: at °C
Description	
Stable	
Deg. product	
Method	
Year	
GLP	
Test substance	: as prescribed by 1.1 - 1.4
Remark	: Estimated by WATERNT program (v. 1.01) from EPIWIN (v. 3.12)
04.15.2006	
Remark	Literature value for pKa 4.3 (Perrin, DD, 1972)

2.6.2 SURFACE TENSION

Type	: Surface Tension
Value	: = 4.856 x 10-2 N/m @ 3.5°C
Method	
Year	
GLP	
Test substance	: as prescribed by 1 .1 - 1.4
Remark	: Literature Value (Daubert, TE,.1989)
04.15.2006	

2.7 FLASH POINT

Type : Flash Point

Value	: = 92°C
Method	: other: TCC
Year	
GLP	
Test substance	: As prescribed by 1.1 ▪ 1.4
Remark	: Albemarle MSDS 04.15.2006

2.8 AUTO **FLAMMABILITY**

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 **OXIDIZING PROPERTIES**

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1 .1 PHOTODEGRADATION

Type	:	Photodegradation
Light source	:	
Light spectrum	:	
Relative intensity	:	
Conc. of substance	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	In general, anilines absorb light in the environmental UV spectrum (> 290 nm). Thus, OEA is expected to absorb light and may potentially undergo direct photolysis. However, OEA is not predicted to partition to the air in significant amounts. Due to the low vapor pressure, the OEA that does occur in the ambient atmosphere will be in the vapor phase. Vapor phase OEA is predicted to degrade in the atmosphere by reaction with photochemically-produced hydroxyl radicals. The half-life for this reaction in air is estimated to be 0.97 hours, calculated from it's rate constant of 1.3 x 10^{-10} cu cm/molecule-set at 25'C.
Remark		Estimated by AOP program (v. 1.91) from EPIWIN (v. 3.12)
14.02.2002		

3.1.2 STABILITY IN WATER

Type	:	Abiotic
t1/2 pH4	:	
t1/2 pH7	:	
	:	
5	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	
Remark	:	OEA is not expected to undergo hydrolysis in the environment due to lack of hydrolyzable functional groups. (Lyman, W.J., 1990)
Test substance	:	
04.15.2006		

3.1.3 STABILITY IN SOIL

Type	:
t1/2 pH4	:
	:
	:
Deg. product	:
Method	:
Year	:
GLP	:
Test substance	:
Remark	
Test substance	

04.15.2006

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	other: absorption/desorption
Media	:	water - soil
Air	:	0.146 % (Fugacity Model Level III)
Water	:	36.8 % (Fugacity Model Level III)
Soil	:	63 % (Fugacity Model Level III)
Sediment	:	0.11 % (Fugacity Model Level III)
	:	
Method	:	EPIWin Level III Fugacity Model
Year	:	
Remark	:	log Koc = 2.155 (EPI Suite model estimated)

04.15.2006

3.3.2 DISTRIBUTION

Remark : Distribution as estimated by PBT Profiler:
Air: 0%
Water: 37%
Soil: 63%
Sediment 0%

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	Aerobic
Inoculum	:	
Deg. product	:	
Method	:	
Year	:	
GLP	:	
Test substance	:	

Remark OEA is not expected to biodegrade fast as predicted using EPIWIN
04.15.2066

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

BCF	**: ca. 4.363**
Elimination	:
Method	: other: estimate
Year	:
GLP	:
Test substance	:
Remark	Estimated using BCF Program (v 2.15) from EPIWIN (v. 3.12)

3.8 ADDITIONAL REMARKS

Remark :

04.15.2006

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: Estimate
Species	: Other: Fish
Exposure period	: 96 hour(s)
Unit	: mg/l
NOEC	
LC50	: = 30.2 mg/l estimated
LC100	
Method	: other:
Year	
GLP	
Test substance	

Remark : Estimated using ECOSAR program (v. 0.99h); aromatic amine class
04.15.2006

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	: Static
Species	: Daphnia magna (Crustacea)
Exposure period	: 48 hour(s)
Unit	: mg/l
NOEC	
EC50	: = 8.05 mg/l
Analytical monitoring	
Method	
Year	
GLP	
Test substance	: as prescribed by 1 .1 - 1.4

Remark : Literature (Maas-Diepeveen, JL, 1986)
04.15.2006

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	: Green Alga
Endpoint	: EC50
Exposure period	: 96hr
Unit	: Mg/l
EC50	: 38 mg/l
Method	
Year	
GLP	
Test substance	: as prescribed by 1 .1 - 1.4

Remark : Literature (Maas-Diepeveen, JL, 1986)
08.02.2002

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type :

Species :
Exposure period :
Unit :
EC50 :
Method :
Year :
GLP :
Test substance :

Remark :
04.15.2006

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.0 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

Remark : .
14.02.2002

5.0 **TOXICOKINETICS,** METABOLISM AND DISTRIBUTION

5.1 .1 ACUTE ORAL TOXICITY

Type	LD50
Value	= 1010 **mg/kg** bw (combined sexes)
Species	Rat
Strain	CD
Sex	male/female
Number of animals	45
Vehicle	None
Doses	0.29, 0.59, 1.17, 2.35, and **4.7 g/kg**
Method	
Year	: 1971
GLP	
Test substance	as prescribed by 1.1 – 1.4
Remark	Ten rats (5 m, 5 f) per group were gavaged with undiluted OEA. Only 5 males were dosed at the 4.7 g/kg level. All animals dosed at 2.35 g/kg died; no animals died at 0.59 g/kg and lower. Seven animals died at the 1.17 g/kg level. Cyanosis was evident in animals within 24 hours of doseing. Survivors had normal coloration within 7 to 10 days. At necropsy, a significant number of animals had enlarged spleens. (Tulane University, for Ethyl Corporation, 1971)
Test condition	
04.15.2006	

Type	: Oral LD50
Value	: 1260 **mg/kg**
Species	: Rat
Strain	
Sex	
Number of animals	
Vehicle	
Doses	
Method	: other: Literature value
Year	
GLP	
Test substance	as prescribed by 1 .1 - 1.4
Remark	Literature value (Lewis, RJ, 1997)
04.15.2006	

5.1.2 ACUTE INHALATION TOXICITY

Type	: Inhalation
Value	: **mg/l**
Species	: Rat
Strain	
Sex	: Male
Number of animals	: 10
Vehicle	
Doses	: 1.07 **mg/l (220** ppm)

Exposure time	:	1, or 4 hours
Method		
Year	:	1971
GLP	:	No
Test substance	:	As prescribed in 1 .1-1 .4
Remark	:	Rats were exposed in a rectangular chamber 34 liters in volume. Vapor was generated by passing air through the compound at a rate of 2.0 liters per minute. There were no deaths in the group of 5 animals exposed for one hour nor in the group exposed to 4 hours to an OEA air concentration of 1.07 mg/l (220 ppm). No signs of toxicity were noted during exposure or in the 14 day recovery period. There were no significant gross pathology differences at necropsy. (Tulane University, for Ethyl Corporation, 1971)
Test condition		. .

04.15.2006

5.1.3 ACUTE DERMAL TOXICITY

Type	:	Dermal LD50
Value	:	0.84 g/kg bw
Species	:	Rabbit
Strain	:	New Zealand White
Sex	:	male/female
Number of animals	:	16
Vehicle	:	Neat
Doses	:	0.35, 0.54, 0.83 and 1.30 g/kg
Method	:	Other:
Year	:	1971
GLP	:	No
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Four rabbits per dose group (two with intact skin sites and two with abraded sites) were used per dose groups ranging from 0.35 g/kg to 1.3 g/kg). Material stayed in contact with skin for 24 hours exposure. All rabbits died at 1.3 g/kg; no rabbits died at 0.54 g/kg or lower. Using the Thompson-Weil method, LD50 was estimated to be 0.84 g/kg with 95% confidence limits of 0.65-l .08 g/kg (Tulane University, for Ethyl Corporation, 1971)

04.15.2006

Remark
08.02.2002

51.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	Rabbit
Concentration	:	0.5 ml
Exposure	:	Semiocclusive
Exposure time	:	24 hours
Number of animals	:	6

Vehicle
PDII : 0.33 (used intact and abraded site scores)
Result
Classification : Not classified as irritant
Method
Year : 1971
GLP : No
Test substance : as prescribed by 1 .1 - 1.4

Remark : OEA was applied to intact and abraded sites for 24 hour contact. Scoring for erythema and eschar and edema were made at 24 and 72 hours. Primary irritation scoure was calculated from intact and abraded skin sites, at both time points. Classification as an irritant, by the criteria at the time of the test, required a score of 5 or more. Since the Primary Irritation Score calculated in this test was 0.33, the material was not considered an irritant. No site or animal had a "positive" score for erythema or edema at any time point.
(Tulane University, for Ethyl Corporation, 1971)

04.15.2006

5.2.2 EYE IRRITATION

Type : Eye Irritation
Species : Rabbit
Number of animals : 6, male and female
Vehicle : None

Result
Classification : Mildly Irritant
Method
Year : 1971
GLP : No
Test substance : As prescribed by 1. l-l .4

Remark : After 24 hours, cornea and conjunctiva showed signs of slight irritation. All treated eyes showed improvement by day 7. Mean score was 24.5 at 24 hours, 19.8 at 48 hours, 16.1 at 72 hours and 3.5 at 168 hours. Interpretation of the test at the time was mild irritation.
(Tulane University, for Ethyl Corporation, 1971).

08.02.2002

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

5.5. GENETIC TOXICITY 'IN VITRO

Type : Ames test
System of testing : Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100
Test concentration : - S9: 5.0, 1.5, 0.5, 0.15 and 0.05 ul/plate;
+ S9: 15, 5, 1.5, 0.5, and 0.15 ul/plate

Cycotoxic concentr.	:	At highest tested concentrations
Metabolic activation	:	with and without S-9 from Aroclor 1254 induced male Sprague Dawley rats
Result	:	Negative
Method	:	other: based on Ames et. al. (1975)
Year	:	1980
GLP		
Test substance	:	as prescribed by 1 .1 ▪ 1.4
Remark	:	(Curren, R.D.,for Ethyl Corporation, 1980)
Test condition	:	Quality Assurance was similar to GLP

94.152006

5.6 GENETIC TOXICITY 'IN VIVO

04.15.2006

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Remark

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Remark

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

Remark :

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.6 REACTIVITY TOWARDS CONTAINER MATERIAL

Curren, RD., "Activity of T1590 in the Salmonella/Microsomal assay for Bacterial Mutagenicity," Microbiological Associates, Ethyl Corporation, sponsor, 1960.

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Hansch, C. Leo, A., and Hoekman, D., "Exploring QSAR - Hydrophobic, Electronic and Steric Constants," Washington, D.C., American Chemical Society, p. 45, 1995.

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Perrin, DD, "Dissociation Constants of Organic Bases in Aqueous Solution," IUPAC Chemical Service: Supplement, 1972, Butterworth, London, No. 4414, 1972.

Tulane University, "Report on the Acute Toxicity of 1 -Ethylaniline," Ethyl Corporation, sponsor, 1971

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT

SUPPLEMENT TO 2,6 MEA IUCLID

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 1200 mg/kg bw (combined sexes)
Species	:	Rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	30 (5 per sex per group)
Vehicle	:	None
Doses		810, 1150, 1635 mg/kg
Method		
Year		1989
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark		All mortality occurred within a 3 day period post dosing. All animals died at the high dose, 1. at low dose, and 4 at middose. Clinical signs (decreased activity, dyspnea, ataxia, oral discharge and prostration) were manifested at all dose levels, persisting for 6 days in most dose groups. LD 50 for males: 1300 (928-I 672) mg/kg; LD50 females 1050 (787-I 313) mg/kg, combined LD50: 1200 (1033-I 367) mg/kg. Animals found dead had irritant effects in the intestine and green or red fluid in the bladder. Several animals in the high dose group had dilated renal pelvis. (Blazcak, DL, 1989a)
Test condition	:	Vehicle: Material gavaged neat with volume adjusted for dose

04.15.2006

5.1.3 ACUTE DERMAL TOXICITY

Type		LD50
Value	:	1900 mg/kg bw
Species	:	Rabbit
Strain		New Zealand white
Sex	:	male/female
Number of animals	:	29 (one low dose female was euthanized for nontest article reasons)
Vehicle	:	None
Doses	:	1200, 1600, 2000 mg/kg; 24 hour contact
Method	:	FIFRA, 81.2 Acute Dermal Toxicity
Year	:	1989
GLP	:	Yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No animals died in the low or mid dose groups. 7 of 10 animals died at 2000 mg/kg. LD50 for males was 1950 (1672-2228) mg/kg; for females: 1850 (1632-2068) mg/kg; and combined: 1900 mg/kg (1747-2053). Severe dermal effects (necrosis followed by eschar) was noted at the dose sites of one mid dose animal. Other signs of gross toxicity in the 2000 mg/kg group

included hypoactivity and decreased food consumption. Other signs in a few animals included ataxia, hypopnea, fecal staining, hypothermia, emaciation, and prostration. Survivors were free of signs by dy 9. Gross abnormalities were noted for the animals necropsied at the conclusion of the 14-day observation period and included accentuated lobular pattern in the liver, discoloration of the intestinal wall, and discolored fluid in the stomach, intestine, and abdominal cavity.
(Blazcak, DL, 1989b)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 2.6 mg/l
Species		Rat
Strain		Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	
Doses	:	2.1-3.2 mg/l
Exposure time	:	4 hour(s)
Method	:	
Year	:	1989
GLP	:	Yes
Test substance		As prescribed in 1 .1-1 .4
Remark	:	Mean exposure concentrations were gravimetrically determined to be 2.1, 2.5, and 3.2 mg/l. Greater than 93% of the aerosol had a mass median aerodynamic diameter of less than 10 microns. Mortality was 0, and 8/10 for the three dose groups. LC50 and 95% confidence limits was calculated to be 2.6 mg/l (2.24-3.22 mg/l). Hypoactivitiy and clear nasal discharge was seen during exposure; salivation, nonresponsiveness, prostration, slow or labored breathing, nasal and eye discharge, and ocular opacity. Surviving animals were gaining weight by day 14 and exceeded preexposure weights. Unscheduled death animals had abnormal liver color, abnormal color testes, abnormal color urine (green). The only treatment related effect seen in animals at scheduled sacrifice was corneal opacity. (Folk, RM, 1989)

5.2.1 SKIN IRRITATION

Species	:	Rabbit
Concentration	:	0.5 ml
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	6 (3 male, 3 female)
Vehicle	:	

PDII

Result	: Non-irritating
Classification	: FIFRA Category IV
Method	: EPA OPPTS 870.2500
Year	: 1999
GLP	: Yes
Test substance	: as prescribed by 1 .1 - 1.4

Remark : Two intact sites on each animal were prepared by clipping the hair. Test article was applied under a semiocclusive dressing for 4 hours. After 4 hours, the test article was gently wiped off the skin with paper towel. 2,6 MEA produced generally mild and transient dermal irritation. Very slight to slight erythema with little or no edema was seen at one or both sites that disappeared within 24 or 48 hours in five of the six animals. One animal continued to have slight irritation until day 10.
(Blazcak, DL, 1989c)

04.15.2006

5.2.2 EYE IRRITATION

Species	Rabbit
Concentration	: Undiluted
Dose	: 0.1 ml
Exposure time	:
Comment	:
Number of animals	: 6 (2 male, 4 female)
Vehicle	: None
Result	: Moderate irritation
Classification	: FIFRA Toxicity Category III
Method	: FIFRA 81.4
Year	: 1989
GLP	: no data
Test substance	: as prescribed by 1 .1 - 1.4

Remark : Due to vocalization in the first animal, a local anesthetic was applied to the remaining animals' eyes prior to test article application. No wash was used immediately after the exposure period, but was used after 24 hours. Moderate to severe, but reversible ocular irritation was produced: all six animals had mild moderate or severe conjunctival irritation, five had corneal opacity and/or ulceration and three had iridal changes. All animals were free of ocular irritation within 2 to 7 days. This was interpreted as moderate irritation or FIFRA III.
(Blazcak, DL, 1989d)

04.15.2006

References:

Folk, R.M., "2-methyl-6-ethylaniline Rat Inhalation LD50," ML-88-297, Monsanto Environmental Health Laboratory, Monsanto Company sponsor, 1989.

Blazcak, D.L., "2-methyl-6-ethylaniline: Acute Oral Toxicity Study in Rats" Studies". BD-88-296, Bio/dynamics, Inc, Monsanto Company, sponsor, 1989a.

Blazcak, D.L., "2-methyl-6-ethylaniline: Acute Dermal Toxicity Study in Rats" Studies". BD-88-296, Bio/dynamics, Inc, Monsanto Company, sponsor, 1989b.

Blazcak, D.L., "2-methyl-6-ethylaniline: Primary Dermal Irritation Study in Rabbits (4 hour exposure/semi-occlusive covering". BD-88-296, Bio/dynamics, Inc, Monsanto Company, sponsor, 1989c.

Blazcak, D.L., "2-methyld-ethylaniline: Eye Irritation Study in Rabbits". BD-88-296, Bio/dynamics, Inc, Monsanto Company, sponsor, 1989d.

IUCLID

Dataset

Existing Chemical	Substance ID: 24549-06-2
CAS No.	24549-06-2
EINRCS Name	6-ethyl-2-toluidine
EINRCS No.	246-309-6
Molecular Formula	C9H13N

Dataset created by: EUROPEAN COMMISSION - European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following *Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances*. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

Creation date:	18-FEB-2000
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Flags:	non-confidential

1.0.1 OECD and Company Information

1.0.2 Location of Production Site

1.03 Identity of Recipients

1.1 General Substance Information

Substance type: organic
Physical **status:** liquid

1.1.1 Spectra

1.2 Synonyms

1-AMINO-2-METHYL-6-ETHYLBENZOL
Source : Bayer AG Leverkusen

2-AMINO-1-METHYL-3-ETHYLBENZOL
Source : Bayer AG Leverkusen

2-Ethyl-6-methyl-aminobenzene
Source : ALBEMARLE S.A. BRUXELLES

2-ETHYL-6-METHYLANILIN
Source : Bayer AG Leverkusen

2-Ethyl-6-Methylaniline
Source : ALBEMARLE S.A. BRUXELLES

2-ETHYL-6-METHYLANILINE
Source : Bayer AG Leverkusen

2-ETHYL-6-METHYLBENZENAMINE
Source : **Bayer AG** Leverkusen

2-Methyl-6-ethylaniline
Source : ALBEMARLE S.A. Brussels

2-METHYL-6-ETHYLANILINE
Source : Bayer AG Leverkusen

6-ETHYL-2-METHYLANILINE
Source : Bayer AG Leverkusen

6-ETHYL-0-TOLUIDINE
Source : Bayer AG Leverkusen

BENZENAMINE, 2-ETHYL-6-METHYL-
source : Bayer AG Leverkusen

MEA
Source : ALBEMARLE S.A. Brussels

0-ETHYL-0-TOLUIDIN
Source : Bayer AG Leverkusen

0-TOLUIDINE, 6-ETHYL-
Source : Bayer AG Leverkusen

1.3 Impurities

1.4 Additives

1.5 Quantity

1.6.1 Labelling

1.6.2 Classification

1.7 Use Pattern

1.7.1 Technology Production/Use

1.8 Occupational Exposure Limit Values

1.9 Source of Exposure

1.10.1 Recommendations/Precautionary Measures

1.10.2 Emergency Measures

1.11 Packaging

1.12 Possib. of Rendering Subst. Harmless

1.13 Statements Concerning Waste

1.14.1 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 2 (water polluting)
Source : Bayer AG Leverkusen

1.14.2 Major Accident Hazards

Legislation:
Substance listed: no
Source : Bayer AG Leverkusen

1.14.3 Air Pollution

1.15 Additional Remarks

Remark: This material is not considered as a hazardous waste or material. Therefore, it may be disposed of as an industrial waste in a manner acceptable to good waste management practice and in compliance with applicable national and/or local regulations. In doing so however, due consideration must be given to the fact that this product is suspected of inhibiting waste water biological treatment systems.
Source : ALBEMARLE S.A. BRUXELLES

1.16 Last Literature Search

1.17 Reviews

1.18 Listings e.g. Chemical Inventories

2.1 Melting Point

Value: ca. -25 degree C
Method: other
GLP: no data
Source : ALBEMARLE S.A. BRUXELLES
(1)

Value: -24 degree C
Source : Bayer AG Leverkusen
(2)

2.2 Boiling Point

Value: ca. 231 degree C at 1013.2 hPa
Year : 1990
GLP: no data
Source : ALBEMARLE S.A. BRUXELLES
(3)

Value: 231 degree C at 1013 hPa
Source : Bayer AG Leverkusen
(2)

2.3 Density

Type: density
Value: ca. .97 g/cm3 at 20 degree C
Year: 1992
GLP: no data
Source : ALBEMARLE S.A. BRUXELLES
(4)

Type: density
Value: .97 g/cm3 at 20 degree C
Source : Bayer AG Leverkusen
(2)

2.3.1 Granulometry

2.4 Vapour Pressure

Value: .063 hPa at 20 degree C
Source : Bayer AG Leverkusen
(2)

Value : ca. .08 hPa at 20 degree C
Year: 1992
GLP: no data
Source: ALBEMARLE S.A. BRUXELLES
(4)

Value: .643 hPa at 50 degree C
Source : Bayer AG Leverkusen

(2)

Value: 11.95 hPa at 100 degree C
Source: Bayer AG Leverkusen

(2)

2.5 Partition Coefficient

log **Pow:** ca. 2.2
Method: other (calculated)
Year : 1973
GLP: no
Remark : The author states that this value was calculated by standard methods.
Source : ALBEMARLE S.A. BRUXELLES

(5)

log Pow: **2.4**
Method: other (calculated): Leo, A.: CLOGP-3.54 MedChem Software 1989. Daylight, Chemical Information Systems, Claremont, CA 91711, USA
Year:
Source : Bayer AG Leverkusen

(6)

2.6.1 Water Solubility

Value : ca. .22 other at 20 degree C
Year: 1990
GLP: no data
Remark : Units are weight percentage.
Source : ALBEMARLE S.A. BRUXELLES

(7)

Value: **2.66** g/l at 20 degree C
Source : Bayer AG Leverkusen

(2)

2.6.2 Surface Tension

2.7 Flash Point

Value: ca. 102 degree C
Type: closed cup
Method: other
Year: 1992
GLP: no data
Remark: PMCC Method.
Source : ALBEMARLE S.A. BRUXELLES

(4)

Value : **105** degree C
Type: closed cup
Method: other: DIN 51758
Year:
Source : Bayer AG Leverkusen

(2)

2.8 Auto Flammability

2.9 Flammability

Result: other
Year: 1990
GLP: no data
Remark: Flammable limits not established.
Source : ALBEMARLE S.A. BRUXELLES

(4)

Result:
Method: other: DIN 51794
Remark: ignition temperature: approx. 460 degree C
Source : Bayer AG Leverkusen

(2)

2.10 Exdosive Properties

2.11 Oxidizing Properties

2.12 Additional Remarks

3.1.1 Photodegradation

3.1.2 Stability in Water

3.1.3 Stability in Soil

3.2 Monitorine Data (Environment)

3.3.1 Transport between Environmental Compartments

3.3.2 Distribution

3.4 Mode of Degradation in Actual Use

3.5 Biodegradation

Type: aerobic
Inoculum: predominantly domestic sewage, adapted
Degradation: 0 % after 30 day
Result: under test conditions no biodegradation observed
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year : 1973 **GLP:** no
Test substance:
Remark: Concentration: 3; 10; 30 mg/l
related to BOD
Source : Bayer AG Leverkusen

(2)

Type: aerobic
Inoculum: predominantly domestic sewage
Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: < 10 % after 28 day
Bfethod: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year : 1989 **GLP: yes**
Test substance: other TS: min. 99 %
Source : Bayer AG Leverkusen

(2)

Type: aerobic
Inoculum: other: mixture of polyvalent bacteria
Concentration : 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: 6.5 % after 28 day
Result: other
Kinetic:

7 day	6.5 %
14 day	17 %
21 day	6.5 %
27 day	3.1 %
28 day	6.5 %

Method : OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1982 **GLP:** no data
Test substance: other TS: 99.1% purity
Remark: This study followed the modified OECD Screening test 301 E guideline (1981). The test organism/system was a mixture of polyvalent bacteria collected on December 22, 1981 from the following sources:
1) the aeration unit of the sewage treatment plant of Rheinfelden (Switzerland)
2) in the river Rhine (Basle City)
3) from a suspension of garden soil (AG Division, Schoren, Basle)
The study was conducted in 2000 ml Erlenmeyer flasks with water meeting the specification of the OECD method 301E guideline. Temperatures were 23 +/- 2 degrees C. Lighting was indirect daylight. Test concentration was 20 mg/liter DOC (nominal). Duration was 28 days. Sodium benzoate was the control substance. Biodegradation of the test article corrected by the blank control and measured as DOC (mg/l) was 6.5% for day 28. Biodegradation of the reference control was 91% by day 7.
It was concluded that the test substance was not readily biodegradable.
Source : ALBEMARLE S.A. BRUXELLES

(8)

3.6 BOD5, COD or BOD5/COD Ratio

3.7 Bioaccumulation

3.8 Additional Remarks

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species : Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit : mg/l **Analytical monitoring: yes**
LC0: 50
LC100: 70.7
Method: other: Letale Wirkung beim Zebrabaerbling, UBA-Verfahrensvorschlag, Mai 1984, Letale Wirkung beim Zebrabaerbling Brachydanio rerio LC0, LC50, LC100, 48-96h
Year: 1989 **GLP: yes**
Test substance: other TS: min. 99 %
Remark: Analytical monitoring: HPLC
Source : Bayer AG Leverkusen

(2)

Type: static
Species : Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC0: 20
Method: other: Bestimmung der akuten Wirkung von Stoffen auf Fische. Arbeitskreis "Fischtest" im Hauptausschuss "Detergentien" (15.10.73)
Year: 1973 **GLP:** no
Test substance:
Source : Bayer AG Leverkusen

(2)

Type: static
Species : Pseudopleuronectes americanus (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit : mg/l **Analytical monitoring:** no
NOEC: ca. 6.25
LC0: ca. 25
LC50: ca. 35
LC100: ca. 50
Method: other
Year: 1983 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Test was conducted in 38 liter aquaria, each containing final volume of 30 liter test solution or control seawater (natural, filtered seawater). Salinity was 31 parts per thousand, and temperatures were 12.1 to 12.5% C. Five fish were in each aquaria; treatments were duplicated. Loading was 0.14 g of fish tissue per liter of seawater. Fish were not fed during the test nor was the aquaria aerated. Acetone was used as solvent. Seawater and solvent controls were tested concurrently. After 24 hours, mortality was 0% in concentrations equal or less than 25 mg/liter. All fish in higher concentrations were dead at 24 hours. No deaths were observed in the final 72 hours of the test. Fish surviving in 12.5 and 25 mg/liter aquaria were lethargic. Fish exposed to 25 mg/liter were not always able to maintain

upright position. Test article was observed to be out of solution as droplets on water surface at 50 and 100 mg/liter throughout the test.
Dissolved oxygen concentrations were 35-458 saturation in the controls and 81-92% saturation in test concentrations after 96 hours. pH after 96 hours was 7.3 in seawater control and solvent controls and 7.8 to 7.9 in test concentrations with live fish.
LC50 values were calculated by binomial probability method (Stephan, C.E., 1977). 24, 48, and 96 hour LC50 values were the same,. and were 35 mg/liter with 95% confidence limits of 25-50 mg/liter.

Source : ALBEMARLE S.A. BRUXELLES

(9)

Type: static
Species : Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit : mg/l **Analytical monitoring: yes**
LC0: 32
LC50: 43.1 - 44
LC100: 58
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1981 **GLP:** no data
Test substance: other TS: 99.1% purity
Remark: This acute toxicity study followed OECD test guideline 203 for static procedures. Rainbow trout (Salmo gairdneri) averaged 58 nun in length, 1.6 grams in weight and were obtained from P.Hohler, CH-4314 Zeiningen. Acclimization took 13 days. Tests were conducted in 15 liter glass aquaria at a loading of 0.54 grams fish per liter. Two aquaria containing 5 fish were used for each test concentration. Nominal concentrations (measured concentrations) on day 0 were 100 (110), 58 (59.3), 32 (30.5), 18 (16.3), and 10 (9.4) mg/liter. Comparable values for day 4 were 100 (85), 58 (52.5), 32 (28.3), 18 (17.3), and 10 (9.0) mg/liter. Test waters were dechlorinated tap water with a hardness of 180.94 mg/liter calcium carbonate. Temperature was 15 +/- 2 degrees C. Light cycle was 16 hours fluorescent light per day. Gentle aeration was done during the test. No mortality was seen at concentrations of 32 mg/liter and below. All fish died at concentrations of 58 mg/liter and above. Slight effects on swimming behavior and moderate effects on equilibrium were noted at 32 mg.liter from 24 hours onward. No effects were noted at the 18 mg/liter concentration at any time point, but slight effects on respiration were noted in the 10 mg/liter concentration at 96 hours only.- Oxygen, pH, and temperature values measured at each time point showed no significant difference in treatment and control aquaria.
LC 50 values were calculated according to Spear-man-Kaerber: 524-530 in D.J. Finney, London (1964). LCO, LC50, and LC100 at 96 hours determined graphically and expressed in nominal concentrations were 32, 44, and 58 mg/liter respectively. LC50 for 96 hours calculated was 43.1 mg/liter. LC 50 graphically and calculated for 24, 48, and 72 hours were all 44 mg/liter and 43.1 mg/liter.

Source : ALBEMARLE S.A. BRUXELLES

(10)

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l **Analytical monitoring:** no
NOEC: 5.8
EC0: 5.8
EC50: 12.8 - 13.5
EC100: 32
Method: other: EPA 660/3-75-009
Year: 1982 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Test system was Daphnia magna Straus 1820. Test article C 25 702 was described as 99.1% pure, with a solubility of 2000 mg/l in water. Tests were conducted in 250 ml beakers with watchglass covers; 100 ml of test solution was added to each test vessel. Temperatures were 20 +/- 1 degree C. Nominal test concentrations were 0, 3.2, 5.8, 10, 18, and 32 mg test article/liter. Twenty animals were tested at each concentration (4 replicates of 5 daphnids each). Light cycle was 16 hours light, eight hours darkness. IC 50 values were calculated according to J. Berkson (JASA 48, 1953, 569-599).

No immobilized daphnids were seen at 3.2 and 5.8 mg/liter. At the end of the test, pH in the 3.2 mg/liter concentrations was 8.4, with 95% oxygen saturation. At 10 mg/liter, 1 daphnid in each of the 4 replicates were immobilized, equalling 20% immobilization. The 18 and 32 mg/liter concentrations had 90 and 100% immobilization respectively. pH at the highest concentration was also 8.2 with 95% oxygen saturation. IC 50 (48 hours, calculated) was determined to be 12.8 mg/liter with 95% confidence intervals of 11.0 to 15.0 mg/liter. Graphically determined, the IC 50 was 13.5 mg/liter.

Source: ALBEMARLE S.A. BRUXELLES

(11)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species : Agmenellum quadruplicatum (Algae)
Endpoint : growth rate
Exposure period: 72 hour(s)
Unit: µg/l **Analytical monitoring:** no
NOEC: ca. 100
LOEC: ca. 500
Method: other
Year: 1978 **GLP:** no data
Test substance: no data
Remark: Static laboratory method. Exposure was from 72 hours to 7 days. Ethanol solvent control did not inhibit growth. Temperature was 28-30 degrees C. Lab conditions for this test referenced as ASP-2 in Agar, Winters et al., Provasoli, et al., 1957. Effect concentration referenced as 100 or 500 ug per disk.
Source : ALBEMARLE S.A. BRUXELLES

(12)

Species : Scenedesmus subspicatus (Algae)
Endpoint: growth rate
Exposure period: 5 day
Unit: mg/l **Analytical monitoring: yes**
EC50: 58
Method: other: AFNOR T 90-304
Year: 1982 **GLP:** no data
Test substance: other TS: 99.1% purity
Remark: Test organism was Scendesmus subspicatus Cambridge 276/20. Study was conducted in accordance with the French " Norme Experimentale" AFNOR-Norm T 90-304. Test vessels were 25 ml; temperature was maintained at 24 +/- 3 degrees C. Solubility of the test substance was indicated as 2000 mg/liter water. Inoculum was 1.07 x 10^6 cells/ml. Nominal (measured day 0) test concentrations were 0, 5.8 (5.2), 10 (9.4), 18, 32 (33), 58, 100 (102), and 162 (166) mg test article/liter. Comparable day 5 values were 5.8 (3.6), 10 , (7.6), 32 (28), and 100 (83) mg/liter. Potassium bichromate was tested at 1.0, 1.5, 2.3 and 3.4 mg/liter. Four replicates were made of each test concentration. Light cycle was 16 hours of 4000 LUX white fluorescent light and 8 hours of darkness. IC values for growth inhibition in percent were calculated according to J. Berkson: JASA, 48, (1953), 569-599. IC 50 (based on nominal concentration) was calculated for the test substance to be 57.3 mg/liter, with 95% confidence limits of 47.7 to 71.7 mg/liter. IC 50 determined graphically was 58 mg/liter. All test concentrations caused some growth inhibition. The 5.8 mg/liter concentration caused 8.1% inhibition; the 162 mg/liter concentration caused 998 inhibition.
Source : ALBEMARLE S.A. BRUXELLES

(13)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species : activated sludge
Exposure period: 3 hour(s)
Unit: mg/l **Analytical monitoring:** no
EC50: 556
EC05 : 187
Method: IS0 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year: 1989 **GLP: yes**
Test substance: other TS: min. 99 %
Remark: Direct weight
Source : Bayer AG Leverkusen

(2)

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit : mg/l **Analytical monitoring:** no
EC0: 100
Method: other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modifiziert
Year: 1973 GLP: no
Test substance:
Source : Bayer AG Leverkusen

(2)

4.5 Chronic Toxicity to Aquatic Organisms

4.51 Chronic Toxicity to Fish

4.5.2 Chronic Toxicity to Aquatic Invertebrates

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

4.6.2 Toxicity to Terrestrial Plants

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

4.7 Biological Effects Monitoring

4.8 Biotransformation and Kinetics

4.9 Additional Remarks

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species : rat
Sex :
Number of Anilnals:
Vehicle:
Value: ca. 1180 mg/kg bw
Method: other
Year: 1972 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Work was conducted at Tulane University School of Medicine, Laboratory of Environmental Medicine, using test article supplied by Ethyl Corporation. Male Sprague-Dawley rats were fasted overnight and intubated with undiluted test article. Animals were observed for 14 days. Severely intoxicated animals were lethargic before recovery or death. Cyanosis of the limbs, mouth and nose was seen in severely affected animals. LD50 values were calculated by the tables of Weil (1952). LD50 and 95% confidence limits in units of grams per kilogram body weight were 1.18 (0.82-1.69).
Source : ALBEMARLE S.A. BRUXELLES

(14)

Type: LD50
Species : rat
sex:
Number of Animals :
Vehicle:
Value: ca. 1150 mg/kg bw
Method: other
Year: 1980 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: This study was conducted in accordance with the proposed EPA guidelines published in Federal Register Volume 43 (163): 27355-37356. Good Laboratory Practices followed EPA regulations in the Federal Register, Vol 44 (91): 27334-27375, 1979.

Sprague Dawley rats in groups of five rats/sex per dose were gavaged with neat test article after an overnight fast. Dose levels were 500, 601, 721, 866, 1041, and 1250 mg/kg. A final mortality of 0, 0, 0, 20, 20, and 60% precluded calculation of an LD50. Further testing used 1140.7, 1501.4, and 1803.4 mg/kg in the same group sizes. Mortality was 30%, 90 and 90% for the additional groups.

Clinical signs observed were mostly decreased activity, decreased muscle tone, and bradypnea. Observations at necropsy included gastric distension and distension of the urinary bladder.

LD50 calculations used the method of Litchfield and Wilcoxin (1949). Combined sex LD50 and 95% confidence intervals were 1150 (1028-1286) mg/kg. For females, the values were 1200 (941-1531) mg/kg; for males, the values

were 1620 (1060-2477) mg/kg.
Source : ALBEMARLE S.A. BRUXELLES

(15)

Type: LD50
Species : rat
Sex :
Number of Animals:
Vehicle:
Value: = 1180 mg/kg bw
Method:
Year: GLP :
Test substance:
Source : Bayer AG Leverkusen

(16)

Type: LD50
Species : rat
Sex:
Number of Animals:
Vehicle:
Value: = 885 mg/kg bw
Method :
Year : GLP:
Test substance:
Source : Bayer AG Leverkusen

(17)

Type: LD50
Species : rat
Sex:
Number of Animals:
Vehicle:
Value: = 1700 mg/kg bw
Method:
Year: GLP :
Test substance:
Source : Bayer AG Leverkusen

(18)

Type: LD50
Species : mouse
Sex :
Number of Animals:
Vehicle:
Value: = 930 mg/kg bw
Method:
Year: GLP:
Test substance:
Source : Bayer AG Leverkusen

(18)

Type: LD50
Species : rabbit
Sex :
Number of Animals:
Vehicle:
Value: **= 700** mg/kg bw
Method:
Year: **GLP :**
Test substance:
Source : Bayer AG Leverkusen

(18)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species : rat
Sex :
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: **>** 260 ppm
Method: other
Year: 1970 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Two groups of 5 male CD rats weighing 200-300 grams each were used: one group was exposed for one hour and the other for four hours in the test chamber. A nominal concentration of 260 ppm test article was established in **a** 34 liter chamber by passing all air flowing into the chamber through a container of the liquid compound at a flow rate of 2 liters per minute. There were no deaths or other signs of toxicity during the exposure periods or during the 14 day, observation period. No significant pathological findings were noted at necropsy.
Source : ALBEMARLE S.A. BRUXELLES

(19)

5.13 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex :
Number of Animals:
Vehicle:
Value: ca. 1290 mg/kg bw
Method: other
Year: 1970 **GLP:** no
Test substance: **as** prescribed by 1.1 - 1.4
Remark: This study used male and female New Zealand Rabbits, 2.3 to 3.0 kg in weight. Undiluted test article was injected onto the skin under plastic sleeves fitted around the animal. Two of the four animals at each dose level had the skin

sites abraded. Doses were 0.83, 1.30, 2.00, and 3.10 grams/kg. No deaths occurred at 0.83 grams per kilogram. Two animals died in the 1.3 gram/kg group on days 4 and 14. All animals died at 2.00 and 3.10 gram/kg within 3 days of dosing. Animals showed definite color change at 24 hours indicative of cyanosis. LD50 values as calculated by the method of Thompson and Weil were 1.29 grams/kilogram with 95% confidence limits of 1.00 to 1.66 grams per kilogram.

Source: ALBEMARLE S.A. BRUXELLES

(19)

51.4 Acute Toxicity, other Routes

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species : rabbit
Concentration:

Exposure :
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: Draize Test
Year : 1970 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark : Six New Zealand Rabbits (male and female in the group) were used in this study. Each animal had 0.5 ml test article applied to each of 4 skin areas, 2 of which were abraded. Each area was then covered with a gauze pad. Observations were made of the skin sites at 24 and 72 hours. All readings were 0.0 at all sites at all time periods. Thus, the Draize score was 0.0.
Source: ALBEMARLE S.A. BRUXELLES

(20)

Species : rabbit
Concentration:

Exposure :
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1981 **GLP:**
Test substance:
Source: Bayer AG Leverkusen

(21)

5.2.2 Eye Irritation

Species : rabbit
Concentration:
Dose :
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.: irritating
Method: Draize Test
Year: 1970 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Male and Female New Zealand White rabbits had 0.1 ml of undiluted test article instilled into one eye. Observations were made 1,2,3 and 7 days after instillation. Mean Draize scores were 26.2, 11.6, 4.7, and 0 for the 1,2,3 and 7 day scoring periods. No animal had a score of greater than 2 for conjunctival redness or swelling at any period. Mean redness scores were 1.3, 0.7, 0.2 and 0 for the four periods. Five of the six rabbits had positive scores for cornea1 opacity at the first reading. Two animals still had cornea1 scores at 3 days, but all were clear at day 7. One animal had an iris score of "1" at the first reading, but all iris scores were "0" at the second reading.
Source : ALBEMARLE S.A. BRUXELLES

(19)

Species: rabbit
Concentration:
Dose :
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1987 **GLP:**
Test substance:
Source: Bayer AG Leverkusen

(21)

5.3 Sensitization

Type: Maurer optimisation test
Species : guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification: not sensitizing
Method: OECD Guide-line 406 "Skin Sensitization"
Year: 1983 **GLP:** yes
Test substance: other TS: technical, 98% purity
Remark: This study used 10 male and 10 female guinea pigs of the Pirbright white strain (Tif:DHP), weighing between 319 and 422 grams, and approximately 10 weeks of age. Animals were acclimatized for 11 days. Induction consisted of a total of 10 intracutaneous injections given every second day (except weekends). Treated animals received injections of freshly prepared 0.1% test article in physiological saline: control animals received vehicle alone. On the first day, 0.1 ml intracutaneous injections were given into the shaved skin of the right flank and the back, while thereafter, a single injection into the back was given. During the second and third week, the test material was incorporated into a mixture of normal vehicle with complete Bacto adjuvant (1:1).

Fourteen days after last induction, a challenge injection of 0.1 ml of a freshly prepared 0.1% solution of test article in physiological saline was administered into the skin of the left flank. Twenty four hours after each injection in the first week of induction, and 24 hours after the challenge injection, skin reactions were recorded. The two largest perpendicular diameters (in mm) and the increase in skin-fold thickness (in mm) were measured and by multiplication of these values a "reaction volume" was obtained (in ul) for each reading from each anima. The mean volume plus one standard deviation of the induction reactions taken in the animal's first week reactions was taken as the skin irritation "threshold" for each animal. Any challenge reaction greater than this threshold was graded as an allergic reaction and the animal termed "positive". The number of positive animals within the test group was compared with the number of positives within the control group that showed non-specific reactions of the same magnitude. (An exact Fisher test for comparison of the basic probability of two binomial distributions, L. Sachs, Statistitiche Auswertungmethoden, 1971; P < or = 0.01 to indicate significant difference).

Ten days after intracutaneous challenge injection, a subirritant dose of test compound (30%) in Vaseline and Vaseline alone was applied to the skin under an occlusive dressing which was left in place 24 hours. Skin reactions were evaluated at 24 and 48 hours according to Draize scoring scale. The control group was treated with Vaseline and (in at least 10 animals) with test article in Vaseline to check subirritant concentration in adjuvant treated animals.

Two animals died during performance of the test Deaths were attributed to lung infections. At the first intradermal injection challenge, seven test article induced animals of 20 had positive scores. No control animal (out of 18) had a positive score.

At the epidermal challenge, no treated animal had a positive score at the 24 or 48 hour readings.

After the end of the standard test, a second intradermal challenge was conducted. Only 1 of 20 animals had a positive score. This was not statistically significantly different from the control group.

It was concluded that the first challenge induction results were nonspecific reactions, and that the test article had no sensitizing potential.

Source : ALBEMARLE S.A. BRUXELLES

(22)

5.4 Repeated Dose Toxicity

Species : rat Sex: male
Strain: Fischer 3.44
Route of admin.: qavaqe
Exposure period: 5, 10 bzw. 20 d
Frequency of treatment :
Post. obs. period: no
Doses : 221
Control Group: other: sham gavage
Method:
Year : GLP:
Test substance:
Result: body and organ weights as well as mortality unchanged, no histopathologic lesions except a minimal increase of the hypercellularity in the bone marrow of those animals which were treated for 10 d
Source: Bayer AG Leverkusen

(17)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
system of testing: Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100 from Dr. Bruce Ames, Berkeley California, USA).
Concentration: 5 ul, 1.5 ul, 0.5 ul, 0.15 ul, 0.005 ul per plate
Metabolic activation: with and without
Result: negative
Method: other
Year: 1980 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: This assay was conducted by the method of Ames, et al, 1975, with modifications of Deserres and Shelby, 1979, and Mattern and Greim, 1978. In the assay with metabolic

activation, S-9 was prepared from adult male Sprague Dawley rats by established methods (intraperitoneal Aroclor-1254). In the test with and without metabolic activation, positive controls for each of the five strains induced revertant numbers per plate at least five times greater than solvent controls. In both tests, all concentrations of test article failed to induce an average number of revertants per plate three times greater than control. Sterility controls for the S-9 mix, positive controls and the test article dilutions were negative for bacterial contamination. Toxicity was not noted in any of the strains at any of the test concentrations.

Source: ALBEMARLE S.A. BRUXELLES

(23)

Type: Ames test
System of testing: S. typhimurium TA 98, TA 100
Concentration:
Metabolic activation: with
Result: positive
Method:
Year :
GLP:
Test substance:
Remark : test substance weakly mutagenic only in strain TA 100; small dose-related increase in the relative mutagenicity below a factor of 2
Source: Bayer AG Leverkusen

(24)

Type: Ames test
System of testing: S. typhimurium
Concentration:
Metabolic activation: with
Result: negative
Method:
Year :
GLP:
Test substance:
Source: Bayer AG Leverkusen

(25)

Type: Ames test
System of testing: S. typhimurium TA 100
Concentration:
Metabolic activation: with and without
Result: negative
Method:
Year:
GLP:
Test substance:
Source : Bayer AG Leverkusen

(26)

Type: Mammalian cell gene mutation assay
System of testing: BALB/3T3 Clone A31 mouse embryo cells derived by T. Kakunaga from Clone A31 of the BALB/3T3 cell line of Aaronson and Todaro.
Concentration: 0.5 ul/ml, 0.25 ul/ml, and 0.1 ul/ml.
Metabolic activation: with and without
Result: negative
Method: other
Year : 1980 GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Remark: These assays were modifications of the method of Schechtman and Kouri (1977). For the activation assay, cells were treated in suspension in a reaction mixture of cofactor pool (NADPH-generating system), S-9, and the test article or control compounds. DMSO was used as the solvent for both assays. The test article failed to induce Type II and Type III foci at the concentrations tested. Criteria for a valid test were met.
Source : ALBEMARLE S.A. BRUXELLES

(27) (28)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species : mouse Sex: male/female
Strain: other
Route of admin.: i.p.
Exposure period: 24 hours
Doses: 0 mg/kg, 10 mg/kg and 80 mg/kg
Result:
Method: other
Year: 1979 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Remark: This test was conducted under Good Laboratory Practices as outlined by the Food and Drug Administriation, Federal Register, Part II of December 22, 1978, Part 58, Title 21.
The test article was administered intraperitoneally once daily for two days to four female and four male CF-1 mice at a high dose of 80 mg/kg; and to a similar group at a low dose of 10 mg/kg. Triethylenemelamine was a positive control at 0.5 mg/kg and 0.25% methylcellulose at 20 ml/kg was a negative control. All mice were sacrificed by inhalation of CO2 six hours after the second dose. The results were considered negative based on the inability of the chemical to produce a statistically significant increase in the number of micronuclei per 1000 polychromatic erythrocytes in the treated versus the control groups.
Source : ALBEMARLE S.A. BRUXELLES

(29)

Type: Micronucleus assay
Species : other: no data Sex: no data
Strain:
Route of admin.: other: no data
Exposure **period:** no data
Doses : no data
Result:
Method:
Year: **GLP:**
Test substance:
Result: Results: negative
Source : Bayer AG Leverkusen

(25)

5.7 Carcinoeenicity

5.8 Toxicity to Reproduction

5.9 Developmental Toxicity/Teratogenicity

5.10 Other Relevant Information

Type: Metabolism
Remark : This study was designed and monitored to comply with Good Laboratory Practices (FDA as in 43 FR 59986 (21CFR 58). The absorption, distribution, elimination, and bioretention of were examined in Fisher 344 rats (50-72 days old at start) treated with 10 daily oral doses of 88.5 mg/kg body weight. Control rats were pretreated with nine daily oral doses of vehicle (0.1 N HCL) followed by a tenth dose of 14C test article. After the last (tenth) dose, levels of radioactivity in blood and excreta were measured for 24 hours, then the animals were sacrificed and the residual radioactivity in tissues was determined. Radioactivity was measured in a liquid scintillation counter. Preliminary studies (in Sprague Dawley rats) showed that a single oral dose of labeled test article was readily absorbed and distributed to various organs and tissues. The compound and/or it's metabolites were eliminated primarily in the urine and to a lesser extent in feces. Excretion in expired air was minor. Only small portions of the administered radioactivity were recovered in blood and tissues at 24 hours after dosing. Residual activity was highest in livers, kidneys, thyroids, adrenals and fat.

Compared to vehicle-pretreated rats, the rats pretreated with labeled test article displayed higher (1.4 to 4.6 times) levels of radioactivity in blood throughout the 24 hour period following the last dose. However, both pre-treatment groups showed similar rates of urinary and

fecal excretion of radioactivity. There was no apparent sex difference in 14C contents of blood and excreta of both treatment groups.

Radioactivity recovered in tissues was highest in livers, kidneys, blood components, fat, adrenals and thyroids. With the exception of fat, residual activity in tissues were higher (1.5 to 6.2 times) in the 14 C test article pretreated rats compared with vehicle pretreated animals. These higher levels were especially apparent in blood, RBC's, spleens, epididymides, uteruses, brains, hearts, muscle, and bone marrow. Females in the two pretreatment groups retained slightly higher levels of radioactivity in most tissues. The amounts of the last (tenth) dose recovered in the 14 C pretreated rats were 2.5 times higher (blood) and 4.5 times higher (tissues) than those of controls, but the 14 C contents of the GI tracts did not differ to a great extent. However, when the retained activity is expressed as percentages of the total (10) administered doses, the recoveries in blood and tissues were lower than those retained in the vehicle-pretreated controls.

source : ALBEMARLE S.A. BRUXELLES

(30)

Type: Metabolism

Remark: The fate of 2-ethyl-6-methyl aniline in rats after oral and dermal application, and after inhalation exposure was followed using randomly 14C labelled material. Rats were strain: Tif:RAI f (SPF). Oral and dennal materials were dissolved' in ethanol and water. Inhalation exposures were nose only. Measured concentrations were 0.3 ug 14C-test article per liter.

Independent of application route, at a dose level of 5 mg/kg (oral), 0.1 mg/kg (oral, dermal), and 0.03 mg/kg (inhalation), the test article was readily taken up into the general circulation and rapidly excreted, mainly via the kidney. (76 to 93% being found in the 24 hour collected urine). Only 2-6% of the dose was eliminated in the feces within 48 hours. In the expired air, no acidic exhalation products were found; whereas 10% of the alkaline volatiles were detected within the first 24 hours in the inhalation study.

About and less than 1% of the dose applied remained in or on the animal after dennal (48 hours), inhalation (48 hours) and oral (72 hours) application.

In the first 24 hour urines, one major metabolite was identified as the sulfate ester conjugate of 2-ethyl-4-hydroxy-6-methyl aniline. Identification was by two-dimensional thin layer chromatography, followed by spectroscopy and NMR analysis of the purified compound. It represents 65% (oral, low dose), 77% (oral, high dose), 60% (dermal) and 51% (inhalation) of the dose.

The test article was administered as the hydrochloride in the dennal and oral studies.

Source : ALBEMARLE S.A. BRUXELLES

(31)

Type:
Remark: single oral administration of 20, 100 or 500 mg/kg bw to male rats: no significant increase of methemoglobin
Source : Bayer AG Leverkusen

(32)

Type:
Remark : Study of the occlusive dermal absorption of 2-ethyl-6-methyl aniline hydrochloride in rats (dose: 0.1 mg/kg bw 14C-phenyl-2-ethyl-6-methyl aniline hydrochloride = MEA): 78.4 % of the radioactive dose are detected in the urine and 2.3 % are found in the feces after 48 h. The main (60 % of dose) urinary component was identified as the sulfate ester conjugate of 2-ethyl-4-hydroxy-6-methylaniline
Source : Bayer AG Leverkusen

(33)

Type:
Remark: 2-methyl-6-ethylaniline was found to be inactive in the cell transformation assay (no further data)
Source : Bayer AG Leverkusen

(25)

5.11 Experience with Human Exposure

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(20) Ethyl Corporation, unpublished data, 1970.
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(21) Bayer AG data, Report No. 17751, 22.2.1989

(22) CIBA-GEIGY, Ltd., unpublished data, "Report on Skin Sensitization Effects in Guinea Pigs C 25 702," Basel, Switzerland, 1983.

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7.1 Risk Assessment